25-HYDROXYVITAMIN D STATUS OF PATIENTS WITH PSORIASIS VULGARIS IN A TERTIARY CARE CENTRE IN SOUTH INDIA – A PILOT STUDY

DISSERTATION SUBMITTED IN PARTIAL FULFILLMENT OF THE RULES AND REGULATIONS FOR THE M.D. BRANCH XX DERMATOLOGY, VENEREOLOGY AND LEPROSY EXAMINATION OF THE TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY TO BE HELD IN APRIL, 2015

CERTIFICATE

This is to certify that the dissertation entitled **"25-hydroxyvitamin D status of patients with Psoriasis Vulgaris in a tertiary care centre in south India – A pilot study"** is the bonafide original work of **Dr. Priya Jeevamani C.**

This study was undertaken at the **Christian Medical College and Hospital, Vellore** from December 2013 to August 2014, under my direct guidance and supervision, in partial fulfillment of the requirement for the award of the **MD degree (Branch XX) in Dermatology, Venereology and Leprosy of the Tamil Nadu Dr. M.G.R. Medical University**.

Guide:	**Principal**	**Head of the Department:**
Dr. Susanne A Pulimood,	**Dr. Alfred Daniel,**	**Dr. Renu George**,
Professor, Department of Dermatology, Venereology & Leprosy, Christian Medical College, Vellore.	Christian Medical College, Vellore.	Professor & Head, Department of Dermatology, Venereology & Leprosy, Christian Medical College, Vellore.

DECLARATION

I hereby declare that this M.D. dissertation entitled **"25-hydroxyvitamin D status of patients with Psoriasis Vulgaris in a tertiary care centre in south India – A pilot study"** is the bonafide work done by me under the guidance of **Dr. Susanne A. Pulimood**, Professor, Department of Dermatology, Venereology and Leprosy, Christian Medical College, Vellore. This work has not been submitted to any other university in part or full.

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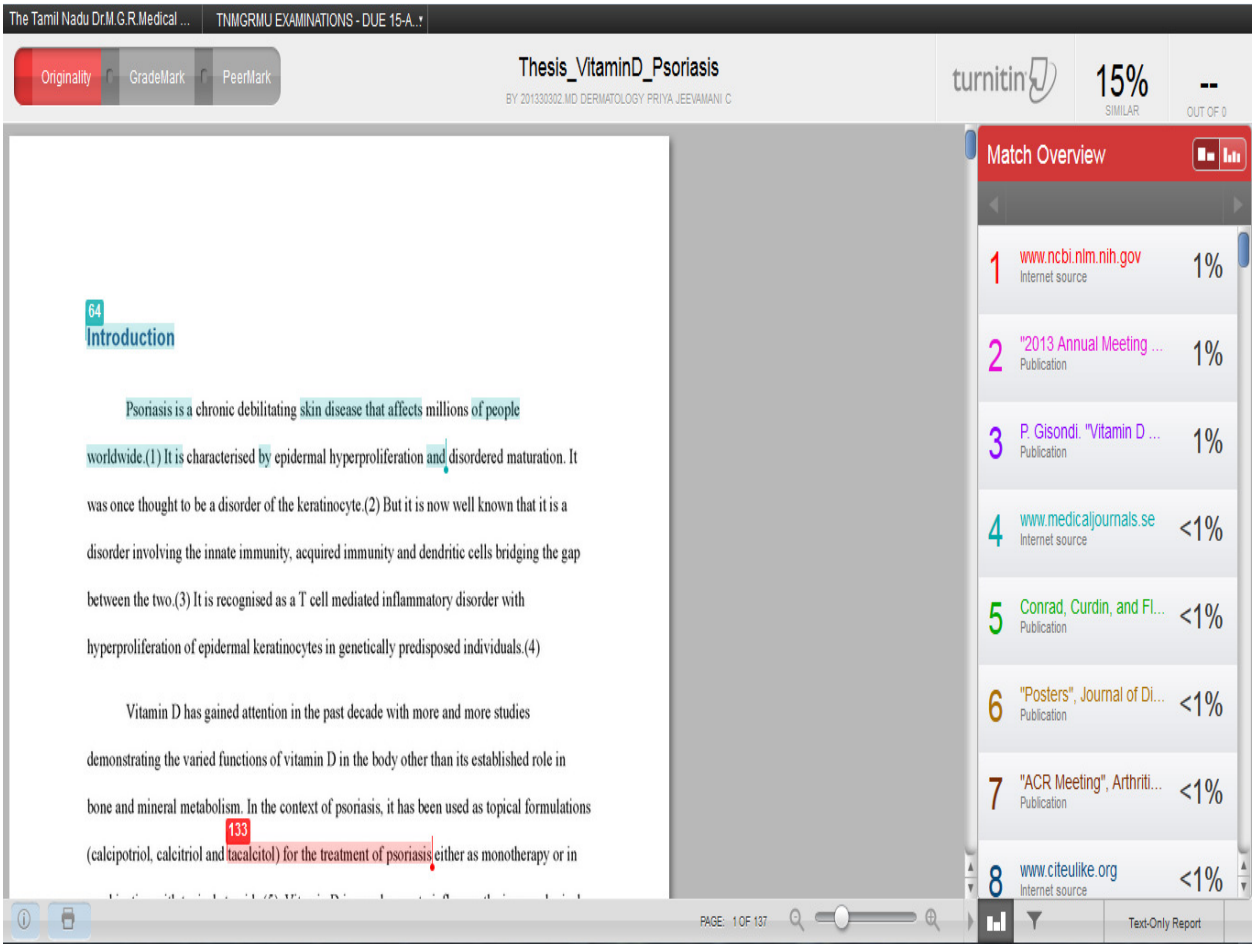
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Introduction
Psoriasis is a chronic debilitating skin disease that affects millions of people worldwide.(1) It is characterised by epidermal hyperproliferation and disordered maturation. It was once thought to be a disorder of the keratinocyte.(2) But it is now well known that it is a disorder involving the innate immunity, acquired immunity and dendritic cells bridging the gap between the two.(3) It is recognised as a T cell mediated inflammatory disorder with hyperproliferation of epidermal keratinocytes in genetically predisposed individuals.(4)
Vitamin D has gained attention in the past decade with more and more studies demonstrating the varied functions of vitamin D in the body other than its established role in bone and mineral metabolism. In the context of psoriasis, it has been used as topical formulations (calcipotriol, calcitriol and
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ACKNOWLEDGEMENT

I wish to record my sincere gratitude to my teacher and guide Dr. Susanne A Pulimood, Professor, Department of Dermatology, Venereology and Leprosy, for her expert guidance, encouragement and support, without whom this dissertation would not have been possible.

Dr. Dincy Peter, Professor, Department of Dermatology, Venereology and Leprosy for her expert guidance, help and encouragement.

My co-guide Dr. Thomas Paul, Professor, Department of Endocrinology, for his expert guidance, encouragement and immense support.

Dr. Renu George, Professor & head, Department of Dermatology, Venereology and Leprosy, for her encouragement and support.

Dr. Leni George, Assistant Professor, Department of Dermatology, Venereology and Leprosy, for her valuable inputs and help in recruitment of patients.

The Assistant Professors, Dr. Anu Anna George, Dr. Nirmal B, tutor, Dr. Anusha, Dr. Gauri and all my co-registrars, with special mention, Dr. Anju Liya & Dr. Priya Kuryan for their support and immense help in recruitment of patients.

Ms. Gowri for her invaluable help with statistical analysis and handling of data.

Mrs. Linda, for her secretarial assistance.

My husband, daughter and mother, for their never ending support and constant encouragement.

All the patients who participated in the study, without whom this dissertation would not have been possible.

The institution for giving me this opportunity, to conduct the study.

Last, but not the least, God the Almighty, for His blessings throughout.

Institutional Review Board approval letter

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December 31, 2013

Dr. Priya Jeevamani
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Sub: **Fluid Research grant project:**
25-hydroxyvitamin D status in patients with Psoriasis Vulgaris in a tertiary care centre in South India – A pilot study.
Dr. Priya Jeevamani, Dermatology, Venereology & Leprosy Unit, Dr. Susanne Pulimood, Dermatology, Venereology & Leprosy Unit, Dr. Thomas V Paul, Dr. Dincy Peter, Dermatology, Venereology & Leprosy Unit 2, Dr. Leni George. Dermatology, Venereology & Leprosy Unit 2, Ms. Mahasampath Gowri S, Biostatistics.

Ref: IRB Min No: 8593 [OBSERVE] dated 04.12.2013

CHRISTIAN MEDICAL COLLEGE VELLORE INDIA

Dear Dr. Priya Jeevamani,

I enclose the following documents:-

1. Institutional Review Board approval 2. Agreement

Could you please sign the agreement and send it to Dr. Nihal Thomas, Addl. Vice Principal (Research), so that the grant money can be released.

With best wishes,

Dr. Nihal Thomas
Secretary (Ethics Committee)
Institutional Review Board

Dr. NIHAL THOMAS
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cc: Dr. Susanne Pulimood, Dermatology, Venereology & Leprosy Unit, CMC.

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Dear Dr. Priya Jeevamani,

The Institutional Review Board (Blue, Research and Ethics Committee) of the Christian Medical College, Vellore, reviewed and discussed your project entitled "25-hydroxyvitamin D status in patients with Psoriasis Vulgaris in a tertiary care centre in South India – A pilot study." on December 4th, 2013.

The Committees reviewed the following documents:

1. IRB application format
2. Curriculum Vitae' Drs. Priya Jeevamani, Susanne Pulimood, Thomas V Paul, Dincy Peter, Leni George, Mahasampath Gowri S.
3. Informed Consent form (English &Tamil)
4. Information Sheet (English &Tamil)
5. Clinical Research Form
6. No of documents 1-5

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The following Institutional Review Board (Blue, Research & Ethics Committee) members were present at the meeting held on December 4th, 2013in the CREST/SACN Conference Room, Christian Medical College, Bagayam, Vellore 632002.

Name	Qualification	Designation	Other Affiliations
Dr. T. Balamugesh	MBBS, MD(Int Med), DM, FCCP (USA)	Professor, Pulmonary Medicine, CMCH.	Internal, Clinician
Dr. Chandra Singh	MS, MCH, DMB	Professor, Urology, CMCH.	Internal, Clinician
Dr. Visalakshi	MPH, PhD	Lecturer, Dept. of Biostatistics, CMC.	Internal, Statistician
Dr. Anup Ramachandran	Ph. D	The Wellcome Trust Research Laboratory Gastrointestinal Sciences, CMCH.	Internal, Basic Medical Scientist
Dr. Rajesh Kannangai	MD, Ph D.	Professor & In-charge Retrovirus Laboratory (NRL under NACO), Department of Clinical Virology, CMCH.	Internal, Clinician
Dr. Srinivasa Babu	M.Sc, Ph.D.	Senior Scientist, Neurological Sciences, CMCH.	Internal, Basic Medical Scientist
Dr. Anand Zachariah	MBBS, PhD	Professor, Medicine, CMCH.	Internal, Clinician
Dr. Vivek Mathew	MD (Gen. Med.) D.M (Neuro) Dip. NB (Neuro)	Professor, Neurology, CMC	Internal, Clinician
Dr. Bobby John	MBBS, MD, DM, Ph D, MAMS	Professor, Cardiology, CMCH.	Internal, Clinician
Mrs. Pattabiraman	B. Sc, DSSA	Social Worker, Vellore	External, Lay person
Mr. C. Sampath	B. Sc, BL	Legal Expert, Vellore	External, Legal Expert

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Dr. Vathsala Sadan	M.Sc, PhD	Professor, Community Health Nursing, CMCH.	Internal, Nurse
Dr. B. J. Prashantham	MA(Counseling Psychology), MA(Theology), Dr. Min(Clinical Counselling)	Chairperson, Ethics Committee, IRB. Director, Christian Counseling Centre, Vellore	External, Social Scientist
Dr. Anuradha Rose	MBBS, MD	Assistant Professor, Community Health, CMCH.	Internal, Clinician
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Dr. Nihal Thomas,	MD, MNAMS, DNB(Endo), FRACP(Endo) FRCP(Edin) FRCP (Glasg)	Professor & Head, Endocrinology. Additional Vice Principal (Research), CMCH. Deputy Chairperson, IRB, Member Secretary (Ethics Committee), IRB	Internal, Clinician

We approve the project to be conducted as presented.

The Institutional Ethics Committee expects to be informed about the progress of the project, any **adverse events** occurring in the course of the project, any **amendments in the protocol and the patient information / informed consent**.

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Dr. B.J. Prashantham, M.A., M.A., Dr. Min (Clinical)
Director, Christian Counseling Center,
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Deputy Chairperson
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Additional Vice Principal (Research)

On completion of the study you are expected to submit a copy of the **final report**. Respective forms can be downloaded from the following link: http://172.16.11.136/Research/IRB_Polices.html in the CMC Intranet and in the CMC website link address: http://www.cmch-vellore.edu/static/research/Index.html.

Fluid Grant Allocation:

A sum of 50,000 INR (Rupees Fifty Thousand only) will be granted for 1 year.

Yours sincerely

Dr. Nihal Thomas
Secretary (Ethics Committee)
Institutional Review Board

Dr. NIHAL THOMAS
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CHRISTIAN MEDICAL COLLEGE VELLORE INDIA

Cc: Dr. Susanne Pulimood, Dermatology, Venereology & Leprosy Unit, CMC

IRB Min No: 8593 [OBSERVE] dated 04.12.2013

Contents

Abbreviations

25-OH vitamin D	- 25-hydroxyvitamin D
AIDS	- Acquired immunodeficiency syndrome
AMP	- Antimicrobial peptides
ART	- Anti retroviral therapy
BMI	- Body mass index
BSA	- Body surface area
BP	- Blood pressure
CASPAR	- Classification of psoriatic arthritis
CI	- Confidence interval
CRP	- C- reactive protein
CPP	- Chronic plaque psoriasis
DNA	- Deoxyribonucleic acid
DVL	- Dermatology, Venereology and Leprosy
HAART	- Highly active antiretroviral therapy
HDL	- High density lipoprotein
HIV	- Human immunodeficiency virus infection
IFN	- Interferon
IL	- Interleukin
IRB	- Institutional Review Board
IU	- International units
MED	- Minimal erythema dose
mRNA	- Messenger ribonucleic acid
NA	- Not available

NAPSI	- Nail psoriasis severity index
OPD	- Outpatient department
OR	- Odds ratio
PASI	- Psoriasis area severity index
PLI	- Psoriasis life impairment
PTH	- Parathyroid hormone
RDA	- Recommended dietary allowance
RNA	- Ribonucleic acid
SD	- Standard deviation
STI	- Sexually transmitted infection
SPF	- Sun protection factor
Th1	- Type 1 helper
TNF	- Tumor necrosis factor
UV	- Ultraviolet
WHO	- World Health Organisation

Title of the abstract	**-** 25-hydroxyvitamin D status of patients with Psoriasis Vulgaris in a tertiary care centre in south India – A pilot study
Department	**-** Department of Dermatology, Venereology and Leprosy
Name of the candidate	**-** Priya Jeevamani C
Degree and subject	**-** MD Dermatology, Venereology and Leprosy
Name of the guide	**-** Dr Susanne A Pulimood

Abstract

Background

Psoriasis is now recognised as a systemic disease centered on inflammation and involvement of cytokines of the Th1 pathway. There are recent studies showing higher prevalence of vitamin D deficiency in patients with psoriasis than in control groups.(10–13) The discovery of the systemic role of vitamin D in the modulation of the immune system especially the Type 1 helper T cell (Th1) pathway suggests that low levels of vitamin D may have important implications in the pathogenesis of psoriasis.

Objectives

Our primary objective was to determine the 25-hydroxyvitamin D status of patients with chronic plaque psoriasis in comparison with age and sex matched controls as a pilot study. Our secondary objective was to correlate the psoriasis disease characteristics with vitamin D level.

Methods

Forty-five consecutive consenting patients with chronic plaque psoriasis and 45 age and sex matched controls with minor dermatological diseases from Tamil Nadu were recruited in this study. Data on demographic profile, sun-exposure, sunscreen usage, smoking, alcohol, type of clothing, waist circumference, vitamin D level, fasting and post prandial sugars, total cholesterol,

triglycerides, LDL and HDL were collected from all study participants. From the patients with psoriasis, data on duration of disease, disease severity as assessed by BSA and PASI, presence of arthritis / nail changes were also collected.

Results

The overall prevalence of vitamin D deficiency (≤ 20ng/ml) in the study subjects was 53.33%. Sixty two per cent cases and 44% controls had vitamin D deficiency with the observed difference not being statistically significant (p value = 0.096). The mean serum vitamin D level was similar among the cases and controls, 21.54 ± 9.41ng/ml and 21.24 ± 10.97 respectively (p = 0.64). There was no statistically significant difference (p = 0.15) in the mean vitamin D level between patients with type 1 psoriasis (19.56 ±9.8 ng/ml) and type 2 psoriasis (25.86 ± 12.99 ng/ml). The mean serum vitamin D level was significantly (p = 0.0001) lower in patients who wore covered type of clothing (14.48 ± 6 ng/ml) when compared to those who wore clothing that allowed more photo-exposure (23.23 ± 10.28 ng/dl). With an increase in disease duration, there was a tendency towards decrease in vitamin D level (r = -0.2978, p = 0.047). There was no correlation between vitamin D level and psoriasis disease severity measures like PASI and BSA involvement, presence of arthritis and nail changes. The BMI (r = -0.300, p = 0.045) and fasting blood sugar (r = -0.319, p = 0.037) showed a negative correlation and the HDL level (r = 0.34, p = 0.026) showed a positive correlation with vitamin D level. Logistic regression analysis did not show any significant changes in vitamin D level attributable to the presence of psoriasis after adjusting for clothing, skin type, locality, occupation, sun exposure and BMI. In addition, the pattern of clothing was observed to be strongly associated with changes in vitamin D level after adjusting for confounders.

Key words – vitamin D, psoriasis, metabolic syndrome

Introduction

Psoriasis is a chronic debilitating skin disease that affects millions of people worldwide.(1) It is characterised by epidermal hyperproliferation and disordered maturation. It was once thought to be a disorder of the keratinocyte.(2) But it is now well known that it is a disorder involving the innate immunity, acquired immunity and dendritic cells bridging the gap between the two.(3) It is recognised as a T cell mediated inflammatory disorder with hyperproliferation of epidermal keratinocytes in genetically predisposed individuals.(4)

Vitamin D has gained attention in the past decade with more and more studies demonstrating the varied functions of vitamin D in the body other than its established role in bone and mineral metabolism. In the context of psoriasis, it has been used as topical formulations (calcipotriol, calcitriol and tacalcitol) for the treatment of psoriasis either as monotherapy or in combination with topical steroids.(5) Vitamin D is now known to influence the immunological function of dendritic cells as well as T cells, which are the key players in the pathogenesis of psoriasis.(6,7) Through vitamin D receptor (VDR), 1,25-dihydroxyvitamin D3 is shown to inhibit the proliferation of cultured human keratinocytes and to induce terminal differentiation of these keratinocytes.(8) Certain types of VDR gene polymorphisms have been found to be associated with psoriasis.(9) There are recent studies showing increased prevalence of vitamin D deficiency in patients with psoriasis when compared to control groups.(10–13)

Psoriasis vulgaris is now also known to be associated with metabolic syndrome. Metabolic syndrome comprises of obesity, diabetes mellitus, hypertension, low levels of HDL and hypertriglyceridemia.(14,15) Studies also show an association between vitamin D deficiency and metabolic syndrome.(16) Psoriasis has been shown to be associated with vitamin

D deficiency even after adjusting for confounders including high body mass index in some studies.(12)

There were no published Indian studies on the association between vitamin D and psoriasis vulgaris at the commencement of this study. However a recent study done from Mumbai, India has shown higher prevalence of vitamin D deficiency among psoriatics as compared to controls.(17) This study was designed to study the association between vitamin D and psoriasis vulgaris in south Indian population.

Aim and Objectives

Aim

To study the 25-hydroxyvitamin D status of patients with psoriasis vulgaris in a tertiary care centre in south India.

Primary Objective

To determine the 25-hydroxyvitamin D status of patients with chronic plaque psoriasis in comparison with age and sex matched controls with non-psoriatic, non-photosensitive skin diseases presenting to the outpatient department (OPD) as a pilot study.

Secondary Objective

To correlate the psoriasis disease characteristics with vitamin D level

Review of literature

Psoriasis is a chronic inflammatory and hyperproliferative skin disorder which is now recognised as a systemic disease. Clinical lesions result from hyperproliferation and abnormality in the differentiation of keratinocytes and epidermal infiltration with inflammatory cells.(18) The pathogenesis of psoriasis is centered on inflammation with involvement of cytokines belonging to Type 1 helper (Th1) pathway. Vitamin D acts on the vitamin D receptor (VDR) to regulate keratinocyte growth and differentiation. The discovery of the role of vitamin D in the modulation of the immune system especially the Th1 pathway suggests that low levels of vitamin D may have important implications in the pathogenesis of psoriasis.(19)

Vitamin D

Vitamin D has gained attention in the past decade with several recent reports showing its varied role apart from the well-established role in bone and mineral metabolism. It is now regarded as a hormone rather than a vitamin. The skin is the sole site of synthesis of vitamin D and skin is also one of its important targets.(20)

The two major forms of vitamin D are vitamin D2 (ergocalciferol) and vitamin D3 (cholecalciferol). They are naturally occurring, biologically inert pre-hormones. To become active they require two successive hydroxylations, first with 25-hydroxylase in the liver, and second with 1–hydroxylase in the kidney, to convert to the biologically active 1, 25-dihydroxyvitamin D3 (calcitriol). Calcitriol and calcidiol (25-hydroxyvitamin D3) are active metabolic products of cholecalciferol.(20)

The human genome has 2,776 positions occupied by the vitamin D receptor (VDR). Therefore 10% of the human genes are responsive to vitamin D directly and/or indirectly.(21) It has been suggested that low levels of vitamin D may have important implications in the pathogenesis of psoriasis as it is involved in the keratinocyte growth and differentiation. It possibly has a role in the immunopathogenesis of psoriasis as it is now known to influence the immune functions of dendritic cells and T cells.(19)

Psoriasis

History

In ancient Greece, skin diseases were categorised into psora, lepra and leichen. Psora meant itch. The Old Testament as well as the works of Hippocrates (460 -377 BC) clubbed leprosy as well as psoriasis together. The term 'Psoriasis' was first used by Galen (133-200 AD), though his description was not consistent with what is called psoriasis now. The patients were stigmatised similar to the lepers.(22) Dr. Robert Willan first recognized psoriasis as a specific clinical entity in 1809 and he described it accurately.(23) Finally, the works of Hebra and Gibert provided important distinction between various papulosquamous disorders.(22) Over years with the better understanding of the immune system and more and more reported systemic associations, it has evolved into a systemic disease rather than one that is confined to the skin.(4)

Epidemiology

The prevalence of psoriasis is varied in different parts of the world. A recent systematic review on the global epidemiology of psoriasis (24) showed the following data (table 1).

Table 1 - Global epidemiology of psoriasis

Epidemiology	Prevalence	Incidence
Children	0% (Taiwan) to 2.1% (Italy)	40.8/100,000 person-years (United States)
Adults	0.91% (United States) to 8.5% (Norway)	78.9/100,000 person-years (United States) to 230/100,000 person-years (Italy)

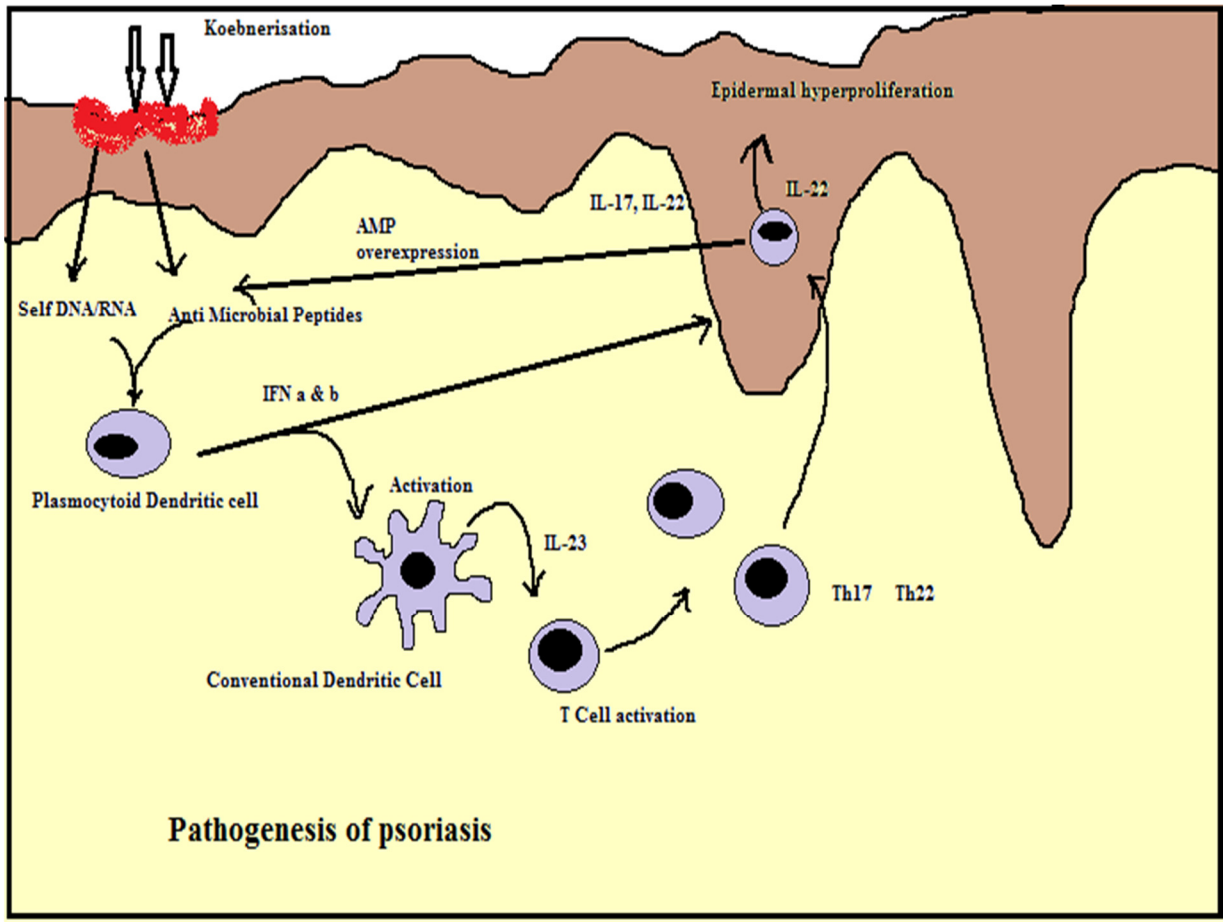
In India, the prevalence of psoriasis ranges from 0.44 to 2.8%. It is twice as common in males as compared to females.(25) Depending on the age of onset, it can be classified into early onset or type 1 disease, when the disease onset is before 40 years and late onset or type 2 disease, when the age of onset is above 40 years.(26)

There are several clinical types, the chronic plaque type being the commonest type reported in up to 90% of individuals with psoriasis. The commonest classification in practice is the one proposed by Griffiths.(27)

Pathogenesis of psoriasis

For long, psoriasis was considered to be a primary keratinocyte disorder. With the effectiveness of cyclosporine, which primarily targets T- cell function in psoriasis, there is a shift in focus from the keratinocyte to the various immunocytes.(3) Understanding the immunopathogenesis of psoriasis helps in the better understanding of the possible link between vitamin D and psoriasis.

The key events involved in the pathogenesis of psoriasis are shown in figure 1.



AMP – Antimicrobial peptides; DNA – Deoxyribonucleic acid; RNA – Ribonucleic acid; IL – Interleukin; Th – T-helper; IFN - Interferon

Figure 1 – Pathogenesis of psoriasis

Upon injury such as in koebnerisation, antimicrobial peptides (AMPs) like cathelicidin LL-37 are produced by keratinocytes. These form complexes with self-nucleic acids (DNA and RNA) released by the injured cells. These complexes lead to the activation of plasmacytoid dendritic cells through endosomal Toll-like receptors 7 and 9. This leads to the production of type I interferons - IFN alpha and IFN beta. This results in maturation and differentiation of conventional dendritic cells. These conventional dendritic cells then stimulate autoimmune T cells through interleukin (IL)-23. These T cells are biased to produce T helper (Th) 17 cytokines

IL-17 and IL-22. These cytokines in turn induce expression of antimicrobial peptides in keratinocytes. This creates a sustained positive feedback loop. In addition, type I IFNs directly upregulate IL-22 receptors on keratinocytes. This increases their responsiveness to IL-22. Interleukin 22 inhibits the terminal differentiation and induces hyperproliferation of keratinocytes. This leads to epidermal hyperplasia which is a hallmark of psoriasis.(3)

In the epidermis, 1, 25-dihydroxyvitamin D_3 and the Vitamin D Receptors (VDR) appear to play a vital role in keratinocyte differentiation. In animal studies, VDR knockout mice exhibited reduced epidermal differentiation marker expression.(28) Vitamin D also has an influence on the immune functions of dendritic cells and T cells which are the key players in the pathogenesis of psoriasis.(19)

Furthermore, vitamin D analogues have been used successfully to treat skin conditions characterised by hyperproliferation, abnormal keratinocyte differentiation and epidermal inflammation.(29)

Vitamin D and dendritic cells

Vitamin D induces tolerogenic responses in conventional dendritic cells. Plasmacytoid dendritic cells from the blood rapidly infiltrate psoriatic skin and as mentioned earlier are important in the initiation of the immunological events in the pathogenesis of the disease. They express various proteins of the VDR pathway, including the vitamin D metabolising enzymes Cyp27B1 and Cyp24A1. Vitamin D receptor is transcriptionally active in plasmacytoid dendritic cells. It is found that vitamin D impairs the capacity of murine and human plasmacytoid dendritic cells to induce T-cell proliferation. It also impairs the secretion of T-helper 1 cytokine IFNγ. This effect is dependent on the expression of the VDR in the dendritic cells. It is proposed that

vitamin D signalling can act as a natural inhibitory mechanism on both conventional and plasmacytoid dendritic cells. This has various pathogenetic and therapeutic implications for psoriasis and other inflammatory skin diseases.(6)

Vitamin D and T cells

In all the stages of a T cell's life, VDR expression and activity are found to be important. This ranges right from development to differentiation as well as the elicitation of effect or functions.(7) Vitamin D inhibits production of interleukin (IL)-2 and IL-6. It blocks the transcription of granulocyte-macrophage colony-stimulating factor mRNA and interferon γ and inhibits cytotoxic T cells and natural killer cell activity.(13)

Vitamin D receptor gene polymorphism and the risk of psoriasis

The vitamin D receptor gene is localized to 12q12-14.(9) Several polymorphisms in VDR gene have been reported. Clinical response to 1∝,25-dihydroxyvitamin D_3 in psoriasis has been found to correlate with the VDR mRNA expression level.(30) This in turn is influenced by the genotype of the VDR. Studies on the association between psoriasis and VDR gene have been performed in four polymorphisms - ApaI, BsmI, FokI or TaqI polymorphisms.(9)

In Northeastern Han Chinese population (31) and Korean population (30) significant association was found between these polymorphisms and psoriasis. A study done in the population of eastern Croatia did not show association between these polymorphisms and psoriasis vulgaris.(32) Data based on meta-analysis showed that ApaI, TaqI polymorphisms in Caucasians,(9) ApaI and FokI polymorphisms in the Turkish populations and BsmI polymorphism in Asians were found to be associated with psoriasis.(33)

Role of vitamin D in the treatment of psoriasis

- Calcipotriol (5)

    - It is a biologically active vitamin D analog which is safe and effective as a topical agent in the treatment of psoriasis. The exact mechanism of action is not known.
    - 1, 25-dihydroxyvitamin D3 receptor expression has been found to increase in epidermal basal keratinocytes during calcipotriol treatment.
    - Studies have shown that the effects on proliferation of epidermal keratinocytes and their differentiation were more than the effects on dermal inflammation.

- Narrow band UVB therapy (34,35)

    - It is a well-established treatment modality for psoriasis.
    - It has been found to increase serum 25-hydroxyvitamin D (25-OH vitamin D) concentration significantly which is now postulated to be one of the possible mechanisms of action of phototherapy in the treatment of psoriasis.

- Oral vitamin D(20)(36)(37)

    - Recent studies show a potential role of oral vitamin D3 supplementation in the treatment of psoriasis.
    - As compared to topical preparations, oral vitamin D is inexpensive and is easily available.

- Some authors recommend monitoring all psoriatic patients for vitamin D deficiency and maintaining normal levels of serum vitamin D.
- It has been proposed that vitamin D in pharmacologic doses could be considered a viable therapeutic option for psoriasis as monotherapy, or in combination with existing treatment options. (20)
- A case of adalimumab-induced psoriasis with resolution of lesions with high vitamin D3 doses has been reported. (36)
- It is proposed that high doses of vitamin D3 may compensate for inherited resistance to its biological effects. (37)

Analysis of 7 prospective trials of oral vitamin D3 supplementation in psoriasis showed its effectiveness and no major adverse effects. Potential side effects of oral vitamin D supplementation include hypercalcemia, hypercalciuria, and renal stones. Long term treatment can also cause bone demineralisation. Though the studies have reported an increase in calcium levels in blood and calciuria, none of the patients experienced adverse clinical events.(38)

Vitamin D deficiency and psoriasis

There are recent studies showing association between vitamin D deficiency and psoriasis (Table 2). In 2011, Gisondi et al. from Italy published the first study showing higher prevalence of vitamin D deficiency in patients with psoriasis as compared to controls.(13) Subsequently studies by Orgaz-Molina et al. from Spain,(11,12) Hesham Abd El-Moaty Zaher et al. from Egypt,(39) Al-Mutairi et al from Kuwait (40) and Gutte et al. from India (17) showed a similar higher prevalence of vitamin D deficiency in psoriatic patients as compared to the controls.

The study by Gisondi et al. was a cross-sectional study conducted in Italy, which included 145 patients with chronic plaque psoriasis, 112 patients with rheumatoid arthritis (considered as positive controls) and 141 healthy controls (considered as negative controls). The prevalence of vitamin D deficiency (< 20 ng/mL) in patients with chronic plaque psoriasis was 57.8% whereas in patients with rheumatoid arthritis and in healthy controls the prevalence was 37.5% and 29.7% respectively ($p< 0.001$).(13)

Orgaz-Molina et al. have published two case-control studies from Spain. In one of the studies, they compared the 25-OH vitamin D status of 43 Caucasian patients with psoriasis (with or without arthritis) with 43 age and sex matched Caucasian controls. The prevalence of vitamin D deficiency (<20 ng/mL) among psoriatic patients was 25.6% and that of the controls was 9.3% ($p <0.043$).(12) In their other study, Orgaz-Molini et al. analysed the 25-OH vitamin D levels of 46 Spanish patients with psoriasis without arthritis and systemic treatment and 46 sex and age matched control subjects. The patients with psoriasis showed significantly lower level of vitamin D than controls (30.5 versus 38.3 ng/ml; $p = 0.0001$).(11)

Hesham Abd El-Moaty Zaher et al. studied the vitamin D status of 48 biopsy-proven psoriatic patients and 40 age, sex and skin phototype- matched controls. Serum 25-OHvitamin D was significantly lower in patients than in controls (21.05 ± 3.66 ng/ml and 37.02 ± 5.06 ng/ml respectively; $p = 0.000$).(39) Al-Mutairi et al from Kuwait studied the serum vitamin D levels of one hundred consecutive patients with stable plaque psoriasis with body surface area involvement ≥10 % with no systemic treatment for 3 months prior to recruitment and compared with equal number of matched healthy volunteers. The serum vitamin D levels of psoriatic

patients were significantly lower than that of the healthy volunteers (31.5 ± 14.41ng/ml versus 53.5±19.6 ng/ml with p <0.005).(40)

Recently in June 2014, Gutte et al. published a prospective case-control study which was conducted in Mumbai on 50 patients with psoriasis and 50 age and sex matched controls. Patients with psoriasis had a 96% prevalence of vitamin D deficiency whereas among controls the prevalence was 64% (p = 0.001). They reported a mean vitamin D level of 13.55±3.43 ng/ml among the patients and in control group it was reported as 20.80±14.37ng/ml (p < 0.001).(17)

However in a population-based study conducted in the United States, they did not find any significant difference in the prevalence of vitamin D deficiency as well as the mean serum vitamin D level between those with self-reported psoriasis and those without the disease. This study included 5,841 participants aged between 20 and 59 years, of which 148 self-reported psoriasis.(41)

Thus the studies showing a higher prevalence of vitamin D deficiency among patients with psoriasis outnumber those that do not show such association. However the possibility of reporting bias cannot be excluded.

Table 2 summarises the reported case-control studies on vitamin D deficiency and psoriasis.

Table 2 – Case-control studies on Vitamin D deficiency and psoriasis

Parameter	Orgaz-Molina et al. (11) Study-1	Orgaz-Molina et al. (12) Study-2	Gisondi et al. (13)	Hesham Abd El-Moaty Zaher et al.(39)	Gutte et. al.(17)
Country	Spain	Spain	Italy	Egypt	India
Vit d deficiency* [Frequency(%)]					
Cases	9 (19.6)	11 (25.6)	81 (57.8)	12 (25)	48 (96)
Control	0 (0)	4 (9.3)	42 (29.7)	0	32 (64)
p- value	.000	0.043	0.001	0.001	0.001
Vitamin D level (mean±SD)ng/ml					
Cases	30.52 ± 9.29	24.41 ± 7.80	20.7 ± 11.3	21.05±3.66	13.55±3.43
Controls	38.31 ± 9.56	29.53 ± 9.38	37.1 ± 27.6	37.02±5.06	20.80±14.37
p- value	0.000	0.007	0.001	0.000	0.001
Overall prevalence of vitamin D deficiency in study subjects	10.98%	17.4%	41.46%	13.64%	80%

**Vit D deficiency – Vitamin D deficiency (<20 ng/ml)*

Correlation of vitamin D level with psoriasis disease characteristics in various studies

- Type 1 and type 2 psoriasis - Park et al. in their study on vitamin D receptor gene polymorphisms (30) have reported a significantly higher frequency of ApaI polymorphism in patients with psoriasis than in healthy controls. This tendency was more accentuated in early onset psoriasis. The other studies on vitamin D and psoriasis did not have the vitamin D correlation with early and late onset psoriasis.
- Duration of disease – Orgaz-Molina et al.(11) as well as Gisondi et al.(13) did not find any correlation of vitamin D level with the psoriasis disease duration.
- Nail psoriasis - The mean 25-OH vitamin D levels did not differ with the presence or absence of nail psoriasis in the study by Orgaz-Molina et al.(12)
- Psoriatic arthritis - In the study by Orgaz-Molina et al., 7% of their patients had psoriatic arthritis and in the study by Gisondi et al., 40.7% of cases had psoriatic arthritis. In both the studies, there was no correlation between the presence of arthritis and vitamin D deficiency.(12,13)
- Psoriasis area severity index (PASI) - Studies by Orgaz -Molina et al.(11) as well as Gisondi et al.(13) did not find any correlation of vitamin D level with PASI.
- Body surface area involvement (BSA) - Similar to PASI, studies have not shown any correlation of vitamin D level with BSA involvement.(11,13)

Correlation of metabolic syndrome related parameters with vitamin D in psoriatic patients in various studies

Apart from the two case-control studies (11,12) mentioned earlier, Orgaz-Molina also studied the vitamin D level of 61 psoriatic patients without arthritis and 61 patients with psoriatic

arthritis. In the psoriatic patients without arthritis, there was inverse correlation between serum 25-OH vitamin D levels and fasting glucose ($r = -0.285$; $p = 0.026$), total cholesterol ($r = -0.440$; $p = 0.000$), triglyceride ($r = -0.280$; $p = 0.029$) values, total cholesterol/high-density lipoprotein ($r = -0.303$; $p = 0.01$) as well as low-density lipoprotein ($r = -0.415$; $p = 0.001$). This association was found to be statistically significant after adjusting for confounding factors in multivariate analysis for total cholesterol, glucose and low-density lipoprotein. However in patients with psoriatic arthritis, they could not find any association between serum 25-OH vitamin D levels and any metabolic parameter. They have suggested a possible protective effect of vitamin-D supplementation in psoriatic patients without arthritis on their metabolic profile.(10)

The same authors, in one of their case control studies observed that the serum vitamin D levels did not correlate with blood pressure, HDL cholesterol, triglycerides or blood sugar levels. They also observed that psoriatic patients with BMI $\geq$ 27 kg/m2 had a higher risk of 25-OH vitamin D insufficiency (sensitivity - 82.3% and specificity - 51.7%) in the same study.(12) In their other case-control study, they observed that the patients with metabolic syndrome had significantly lower serum levels of 25-OH vitamin D than those without metabolic syndrome (24.1 ± 7.5ng/ml vs. 32.8 ± 8.9ng/ml, $p = 0.007$). They found a negative correlation between waist circumference, triglyceridemia, diastolic blood pressure, fasting glucose and the serum levels of 25-OH vitamin D.(11)

Correlation of vitamin D with psoriasis after adjusting for confounders

In the study by Gisondi et al., vitamin D deficiency was found to be associated with psoriasis independently of age, sex, body mass index, season of blood sampling, calcium and

PTH levels in the logistic regression analysis. However since it was a cross-sectional study design, a causal or temporal relationship between psoriasis and vitamin D deficiency could not be commented.(13) Orgaz-Molina et al. found a strong association between psoriasis and vitamin D insufficiency (<30 ng/mL), even after adjustment for confounders like body mass index (BMI), age, sex, Fitzpatrick skin phototype, dietary vitamin D intake, total sun-exposure using multivariate studies with binary logistic regression (Odds ratio 2.89, 95% Confidence interval 1.02-7.64, p <0.03).(12)

Interleukin 17 level and 25-OH vitamin D level in patients with psoriasis

Since psoriasis is considered a prototypic Th17-mediated disease with a possible role played by vitamin D deficiency in its pathogenesis, Hesham Abd El-Moaty Zaher et al assessed the Interleukin 17 levels and 25-OH vitamin D level in patients with psoriasis and age and sex matched controls. Subjects with presence of any condition that might affect interleukin (IL)-17 levels or serum vitamin D levels were excluded from the study. Mean serum 25-OH vitamin D was significantly lower in patients than in controls and serum IL-17 was found to be significantly higher in patients than in controls. No significant correlation was found between vitamin D and IL-17. This controversy was thought to be due to the smaller sample size and the multifactorial aetiology of psoriasis.(39)

Interleukin-17 is proacanthotic, proangiogenic and proinflammatory. Vitamin D promotes differentiation and is antiangiogenic and anti-inflammatory. They seem to have important and opposing roles in innate and adaptive immunity. Vitamin D is believed to inhibit Th17 cell function and thus suppress its downstream cytokines. Their interaction may have a vital role in

the pathogenesis of psoriasis. Hesham et al. proposed that low vitamin D levels could be attributed to the inflammatory milieu that was created by IL-17.(39)

Correlation of vitamin D level and cathelicidin level in psoriatic patients

Cathelicidin (LL-37) is known to initiate an autoimmune response in the pathogenesis of psoriasis by activating plasmacytoid dendritic cells of skin.(42) Vitamin D is now known to regulate the expression of cathelicidin. A study estimating the levels of cathelicidin and vitamin D in psoriasis patients with co-morbidities in comparison with matched healthy controls. The serum vitamin D levels were significantly lower in patients than in controls and the levels of serum cathelicidin were significantly higher.(40)

Metabolic syndrome – The common link between vitamin D deficiency and psoriasis

Metabolic syndrome was first described by Gerald Reaven, an endocrinologist in1988. The original description was the clustering of four conditions namely glucose intolerance, hypertension, central obesity and dyslipidemia in one individual that increased the risk of cardiovascular disease.(43) According to the new International Diabetes Federation: (44)

- One fourth of world's adults have metabolic syndrome.
- Individuals with metabolic syndrome have two times higher risk of mortality and three times more risk of a cardiac attack or stroke when compared to those without the syndrome.
- Individuals with metabolic syndrome have a five times higher risk of developing type 2 diabetes.

- Out of the 200 million individuals with diabetes globally, up to 80% are likely to die of cardiovascular disease.

- This puts diabetes and metabolic syndrome way ahead of HIV/AIDS in terms of morbidity and mortality, however the problem is not as well recognised.

Metabolic syndrome and psoriasis

There are reports suggesting an association of metabolic syndrome with vitamin D deficiency as well as with psoriasis vulgaris. Metabolic syndrome shares some common immunological mechanisms with psoriasis. Since 1950, there are various studies which describe the link between individual components of metabolic syndrome with psoriasis.(43)

The intra-abdominal fat cells secrete adipocytokines thus acting as an endocrine organ. These adipocytokines affect glucose metabolism, promote inflammation and also affect vascular endothelial biology. Visceral adiposity is found to be associated with elevated levels of interleukin-6 (IL-6), tumor necrosis factor alpha (TNF-α), and plasminogen activator inhibitor type1. The levels of TNF-α, IL-6 and plasminogen activator inhibitor type1 have been found to be elevated in psoriasis as well. Leptin is a hormone secreted by adipocytes. It plays a pro inflammatory role in regulating cytokine expression which modulates the Type 1 and Type 2 helper cells. Hyperleptinemia is found to be associated with the development of metabolic syndrome. Elevated levels of leptin has been observed in patients with psoriasis.(45) Adiponectin is another circulating hormone that is produced by adipocytes. It suppresses the production of TNF-α, IL-6 and INF-α and thereby has anti-inflammatory activity. It has anti atherogenic effects and improves insulin sensitivity. Visceral obesity causes hypoadiponectinemia, which in turn increases the cardiovascular risk. The proinflammatory cytokines TNF- α, IFN- α, IL-1, and

IL-6, favor the development of psoriasis as well as atherosclerosis. Osteopontin is an inflammatory glycoprotein which exerts a Th1 cytokine effect. It is thought to play a role in atherogenesis. Psoriasis is found to be a risk for elevated levels of osteopontin.(46)

Hyperinsulinemia in metabolic syndrome has been thought to promote psoriasis susceptibility and / or severity by facilitating angiogenesis and chronic inflammation. In addition, certain pleiotropic genetic loci, e.g., CDKAL1, PSORS2-4, and ApoE4 have been thought to play a role in the shared genetic susceptibility to both metabolic syndrome and psoriasis.(47,48) Obesity is considered to be a risk factor for future development of psoriasis based on several studies and the estimated new cases being attributable to obesity is 30%. Similarly studies show that psoriasis patients are also prone to the future development of components of metabolic syndrome.(15)

April W. Armstrong et al. performed a systematic review and meta-analysis on the epidemiologic associations between metabolic syndrome and psoriasis. The pooled odds ratio for metabolic syndrome among psoriatic patients was 2.26 (95% confidence interval 1.70-3.01) when compared with general population. There are no studies on the incidence of metabolic syndrome among psoriatic patients. The patients with more severe psoriasis were found to have greater odds of metabolic syndrome as compared to those with milder psoriasis.(49)

In a study reported from south India by Shraddha Madanagobalane et al., the prevalence of metabolic syndrome in psoriatic patients was 44.1% whereas in controls it was 30%, the difference being statistically significant (p value = 0.025). The prevalence of triglyceridemia in patients was 33.9% and in controls was 20.8% (p value = 0.011) and that of abdominal obesity was 34.7% and 32.5% (p value = 0.035) respectively. There was no significant difference in the

HDL levels and presence of hypertension among patients and controls. In that study, there was no correlation between the duration and the severity of psoriasis with metabolic syndrome. They suggested that all patients with psoriasis irrespective of the disease severity must be evaluated for metabolic syndrome.(45)

There are also several studies on cardiovascular events in patients with psoriasis. A meta-analysis of both cohort studies and cross-sectional studies showed an increased risk of myocardial infarction with odds ratio of 1.25 (95% CI 1.03–1.52) in psoriasis and 1.57 (95% CI 1.08–2.27) in psoriatic arthropathy when compared with the general population. The risk was found to be more with severe psoriasis and psoriasis with early onset.(50)

Vitamin D and metabolic syndrome

Common obesity and metabolic syndrome has been proposed to result from an abnormal adaptive winter response. A fall in vitamin D is proposed to be the stimulus for the winter response. Vitamin D synthesis is dependent on the absorption of UVB radiation. It has been proposed that vitamin D evolved as a UVB sensitive photoreceptor in primitive organisms and it signals changes in sunlight intensity. A fall in vitamin D is thought to evoke the stimulus for the winter response, which causes an accumulation of fat mass and induction of a winter metabolism. The increasing prevalence of obesity can probably be reversed by improving the vitamin D status.(51)

Vitamin D is thought to play a role in lipogenesis as well as lipolysis regulation as suggested by the presence of vitamin D receptors in adipocytes. Wortsman et al. studied the role of obesity in altering the production of vitamin D3 in the skin as well as its role in intestinal absorption of vitamin D2 (ergocalciferol). In their study obese subjects had lower basal 25-

hydroxyvitamin D levels and higher parathyroid hormone levels than did age matched controls. They evaluated the blood vitamin D3 levels 24 hours after whole body irradiation. The incremental increase in vitamin D3 was 57% less in obese patients than in controls. The content of 7-dehydrocholesterol (vitamin D3 precursor) as well as its conversion to previtamin D3 post irradiation in vitro did not differ significantly between groups. Both the groups were given 50,000 IU of oral vitamin D2. BMI inversely correlated with peak serum vitamin D2 levels after vitamin D2 intake. They concluded that obesity associated vitamin D insufficiency is probably due to decreased bioavailability of vitamin D3 from dietary and cutaneous sources because of its deposition in body fat compartments.(52)

In a study from Saudi Arabia aimed at determining whether vitamin D status correction could reverse the already established manifestations of metabolic syndrome, they recruited a total of 59 adults (31 male, 28 female) who were overweight and obese without diabetes. This was a 1-year prospective, interventional study. Anthropometry measures were recorded. Fasting blood glucose, lipid profile, serum 25-hydroxyvitamin D level, calcium and phosphorous concentrations were measured. Subjects were advised to increase the dietary intake of vitamin D rich food, to do exercise regularly and regularly expose them to sunlight. All measurements were checked 6 and 12 months later. The overall prevalence of metabolic syndrome had decreased from 25.2% to 13.0%. This was mainly contributed by a parallel decrease in the prevalence of triglycerides, low HDL cholesterol and hypertension. They proposed that optimisation of vitamin D status through increased intake of a vitamin D rich diet and increased sun-exposure can lead to an improved cardio metabolic profile. This offers a promising non-pharmacologic approach to the prevention of metabolic syndrome.(53)

Vitamin D deficiency in other disorders

Vitamin D deficiency has been studied in the context of various other disorders, some of which are listed below.

- Cardiovascular disease (54,55) - survival was found to be significantly lower in subjects with vitamin D deficiency.
- Glucose intolerance, type 1 & type 2 Diabetes mellitus (56,57) - increased risk for insulin resistance and metabolic syndrome with vitamin D deficiency and correlation of glycaemic control with vitamin D levels.
- Autoimmune disorders (58) like autoimmune encephalomyelitis, multiple sclerosis, rheumatoid arthritis, systemic lupus erythematosus and inflammatory bowel disease - loss of self-tolerance with vitamin D deficiency.
- In human immunodeficiency virus (HIV) infection (59) – increased risk of vitamin D deficiency and decreased bone mineral density in patients on highly active antiretroviral therapy (HAART) .
- Critical care population (19) – increased mortality with vitamin D deficiency.
- Other dermatological conditions (60–62) like urticaria, vitiligo, atopic dermatitis, etc.- correlation with vitamin D deficiency noted.

Factors affecting the vitamin D status

Vitamin D deficiency/ insufficiency are reported in epidemic proportions worldwide. It is estimated that worldwide one billion people have vitamin D deficiency or insufficiency.(63)

There is slight variation in the interpretation of 25-OH vitamin D serum levels as by various organisations. The recommendation by various organisations (64) is as shown in table 3:

Table 3 – 25-hydroxyvitamin D range guidelines from various organisations

	Endocrine Society	Food and Nutrition Board	Vitamin D Council	Testing Laboratories
Deficient	0-20 ng/ml	0-11 ng/ml	0-30 ng/ml	0-31 ng/ml
Insufficient	21-29 ng/ml	12-20 ng/ml	31-39 ng/ml	…
Sufficient	30-100 ng/ml	>20 ng/ml	40-80 ng/ml	32-100 ng/ml
Toxic	---	---	>150 ng/ml	---

Cutaneous synthesis of vitamin D

Cutaneous synthesis of vitamin D with exposure to ultraviolet radiation accounts for more than 90% of the total vitamin D synthesis in the body.(12) Large quantities of the provitamin D3 molecule 7-dehydrocholesterol is produced in the skin. It is incorporated into the lipid bilayer of plasma membrane of cells in epidermis and dermis. With sun-exposure, UVB radiation in the range of 290–315 nm is absorbed by this 7-dehydrocholesterol. The energy thus absorbed leads to break and rearrangement of chemical bonds within the 7-dehydrocholesterol molecule. This results in the formation of previtamin D3. This previtamin D3 rapidly undergoes thermally-induced transformation to form vitamin D3. Previtamin D3 and vitamin D3 continue to engage in absorption of UV radiation in a wide wavelength range. This continuous absorption of UV radiation results in breakdown of previtamin D3 and vitamin D3 molecules into photoproducts that are biologically inert.(65) During prolonged sun-exposure this results in a

steady state in which only 10–15% of 7-dehydrocholesterol is converted to previtamin D3.(66) This prevents the synthesis of toxic levels of vitamin D3 during prolonged sun-exposure.

Vitamin D3 that is synthesized in the skin is released from the plasma membrane which enters the systemic circulation. It is bound to vitamin D-binding protein once it reaches the circulation.(67) Serum vitamin D3 level peaks 24 to 48 hours after sun-exposure. The serum half-life of vitamin D3 ranges from 36 to 78 hours and the level decreases exponentially.(68,69) Since it is fat-soluble, vitamin D3 is taken up by adipocytes and is stored in subcutaneous as well as omental fat for later use. This prolongs its total-body half-life to nearly two months.(70)

It is further metabolised to 25-OH vitamin D in the liver and 1, 25-dihydroxy vitamin D in the kidneys by subsequent hydroxylations to be converted into active form.

This biosynthesis of vitamin D in the skin is affected by the following factors:

- Exposure to ultraviolet radiation, which is influenced by factors such as the pollutants in the atmosphere and solar zenith angle which is determined by the time of the day, time of the year and latitude
- Cutaneous factors such as clothing, sunscreen usage, Fitzpatrick skin phototype and temperature of the skin (63)
    - Lightweight, loosely woven, white, non-synthetic fibers such as cotton and linen are less effective at blocking UV radiation than thick, densely woven, black and fabrics such as wool, silk, nylon and polyester
    - A sunscreen with sun protection factor 8, if applied in an ideal way is able to prevent the absorption of ultraviolet radiation by 95%

- Darkly pigmented skin with higher concentration of melanin require longer duration to synthesize an equivalent amount of vitamin D3 as compared to individuals with lightly-pigmented skin.(71)

Dietary factors

The Food and Nutrition Board recommended dietary allowance (RDA) for infants below one year of age is 400 IU daily. Between 1 and 70 years of age, the RDA is 600 IU. For elderly over 70 years of age, it increases to 800 IU.(72)

The food and nutrition board recommended dietary allowance is as shown in table 4 below:

Table 4 - The Food and Nutrition Board recommended dietary allowance

Age group	RDA
< 1 year	400 IU
1 to 70 years	600 IU
>70 years	800 IU

Very few food items contain vitamin D. Fish liver oils and flesh of fatty fish such as mackerel, salmon, tuna etc. are the best sources of vitamin D. Small quantities of vitamin D are also found in beef liver, egg yolk and dairy products. In some countries milk and few other food stuff are fortified with vitamin D by law.(72) However in India, dairy products are very rarely

fortified with vitamin D and the very few products that are fortified are not priced within the common man's reach.(73)

Vitamin D deficiency in India

Vitamin D deficiency has a prevalence of 70 to 100% in the Indian subcontinent. It prevails as an epidemic, prevalent in both rural and urban settings, and all socioeconomic groups and geographic strata. In India, dairy products are rarely fortified with vitamin D and the culture and many socioreligious practices do not favor adequate sun-exposure despite the presence of plentiful sunshine. Subclinical vitamin D deficiency is thought to play an important role in the high prevalence of rickets, cardiovascular diseases, diabetes, osteoporosis, cancer and infections like tuberculosis in India.(73) The following factors are thought to play a major role in the high prevalence of vitamin D deficiency.(74)

- Low intake of low dietary vitamin D and calcium can be attributed to changing food habits.
- High fibre diet containing phytates and phosphates can deplete vitamin D stores and increase calcium requirement.
- Genetic factors like the presence of increased 25(OH) D-24- hydroxylase that degrades 25-OH vitamin D to inactive metabolites.
- Increase in serum 25-OH vitamin D in response to treatment depends on heritability of vitamin D binding protein.
- The average number of hours spent outdoor have decreased which prevents adequate sun-exposure especially in the urban Indians.

- Increase in pollution can hinder the ultraviolet rays from adequate synthesizing of vitamin D in the skin.
- Certain religious practices like “Burqa” and the “pardah” system do not allow adequate sun-exposure.
- Absence of adequate spacing between pregnancies can cause vitamin D deficiency in the mother and fetus.

Use of vitamin D in various disorders

There is growing literature on the use of vitamin D in various disorders. A Mayo Clinic monograph on vitamin D use has categorised the scientific evidence of its use as given below(75):

A - Strong scientific evidence

B - Good scientific evidence

C - Unclear scientific evidence

D - Fair scientific evidence against use (might not work)

F - Strong scientific evidence against use (likely does not work)

A	- Familial hypophosphatemia - Fanconi syndrome - Osteomalacia - Rickets - Psoriasis - Hypocalcemia-post parathyroidectomy - Secondary hyperparathyroidism due to deficiency of vitamin D
B	- Dental Cavities - Fall prevention and fracture reduction - Muscle weakness / myalgia - Osteoporosis - Renal osteodystrophy

C	- Asthma - Autoimmune diseases including Crohn's disease, rheumatoid arthritis and multiple sclerosis - Chronic kidney disease – to increase bone density - Cancer prevention (colorectal, breast, prostate, other) - Alzheimer's disease - Infertility - Fibromyalgia - Fracture prevention and treatment - Hepatic osteodystrophy - Hypertension - HIV - Infectious diseases - Increasing lifespan - Inflammatory bowel disease - Loose teeth - Mood disorders including seasonal affective disorder, premenstrual syndrome and depression - Multiple sclerosis - Muscle wasting - Myelodysplastic syndrome - Osteoarthritis - Osteogenesis imperfecta - Steroid induced osteoporosis - Respiratory tract infection prevention - Senile warts - Sexual dysfunction - Stroke - Tuberculosis - Type 1 & type 2 diabetes mellitus - Vitiligo - Post menopause weight gain
D	- Atopic eczema - Prostate cancer treatment - Heart disease - Hypercholesterolemia

In summary the association between the vitamin D status and psoriasis could be relevant for several reasons:

a) It is implicated in keratinocyte differentiation, immune function of T-cells and dendritic cells having important role in the pathogenesis of psoriasis.

b) It has a role in the treatment of psoriasis.

c) It is associated with metabolic syndrome which is known to be common in individuals with psoriasis.

d) Vitamin D receptor gene polymorphisms have been observed in patients with psoriasis.

Thus there appears to be a strong association between vitamin D status and psoriasis vulgaris. There were no Indian studies on the association between vitamin D status and psoriasis vulgaris when we commenced this study.

Considering the high prevalence of vitamin D deficiency in India, a study with larger sample size would be needed. However due to time and financial constraints, this study was designed as a pilot study to help us design further larger trials.

Materials and methods

Study Design:

This was a hospital based, cross-sectional observational case-control study.

Setting:

The study was done in the Dermatology, Venereology and Leprosy outpatient department of our tertiary care hospital. It is a 2122 bedded hospital located in Tamil Nadu, south India.

Study period:

The study was conducted between December 2013 and August 2014.

Participants:

All consecutive patients hailing from Tamil Nadu with chronic plaque psoriasis as the cases and those with non-psoriatic non-photosensitive minor skin problems like warts, naevi, seborrheic keratosis etc. as the controls, attending Dermatology outpatient department during the study period (between December 2013 and August 2014) were considered for eligibility into the study. Patients from only Tamil Nadu were recruited in the study to avoid regional variability in the sun-exposure affecting the vitamin D level. Tamil Nadu extends roughly between the 8° 04' N latitude and the 78° 0' E longitude.

We did not take a community based healthy controls since a community based control would be homogenous in terms of being either a rural area or an urban area. If a rural area is selected, the chances of most people working outdoor and thereby increased sun-exposure would be high. On the other hand, if an urban area is selected, indoor workers may be more and this

would affect the vitamin D level. Hence an OPD based control group coming for minor skin diseases were taken as controls to maintain a heterogenous group as the cases.

Inclusion criteria for cases:

- Age ≥ 18 years and ≤ 65 years
- Chronic plaque psoriasis patients with or without arthritis attending Dermatology outpatient department
- Patients from Tamil Nadu

Exclusion Criteria for cases:

- Psoriasis patients in remission (without skin lesions)
- Oral vitamin D therapy (past or present), topical vitamin D or phototherapy or systemic therapy for psoriasis in the last 3 months
- Other clinical forms of psoriasis like erythrodermic psoriasis, pustular psoriasis
- Presence of chronic inflammatory diseases and autoimmune disorders such as vitiligo, immunobullous disorders, multiple sclerosis, inflammatory bowel disease, rheumatoid arthritis, insulin dependent diabetes mellitus, lupus erythematosus, cutaneous lymphoma, renal disorders, non-melanoma skin cancer or any other cancer
- Patients not willing to participate in the study
- Patients who were not able to give informed consent
- Pregnancy and lactation

Inclusion criteria for controls:

- Age ≥18 years and ≤ 65 years
- Patients with non-psoriatic, non-photosensitive minor skin disorders attending Dermatology outpatient department
- Patients from Tamil Nadu

Exclusion criteria for controls:

- Vitamin D therapy in the past or present
- Presence of chronic inflammatory diseases and autoimmune disorders such as vitiligo, immunobullous disorders, multiple sclerosis, inflammatory bowel disease, rheumatoid arthritis, insulin dependent diabetes mellitus, lupus erythematosus, cutaneous lymphoma, renal disorders, non-melanoma skin cancer or any other cancer
- Patients not willing to participate in the study
- Patients who were not able to give informed consent
- Pregnancy and lactation

The process that was followed in our study for the recruitment of cases and controls is shown in figure 2.

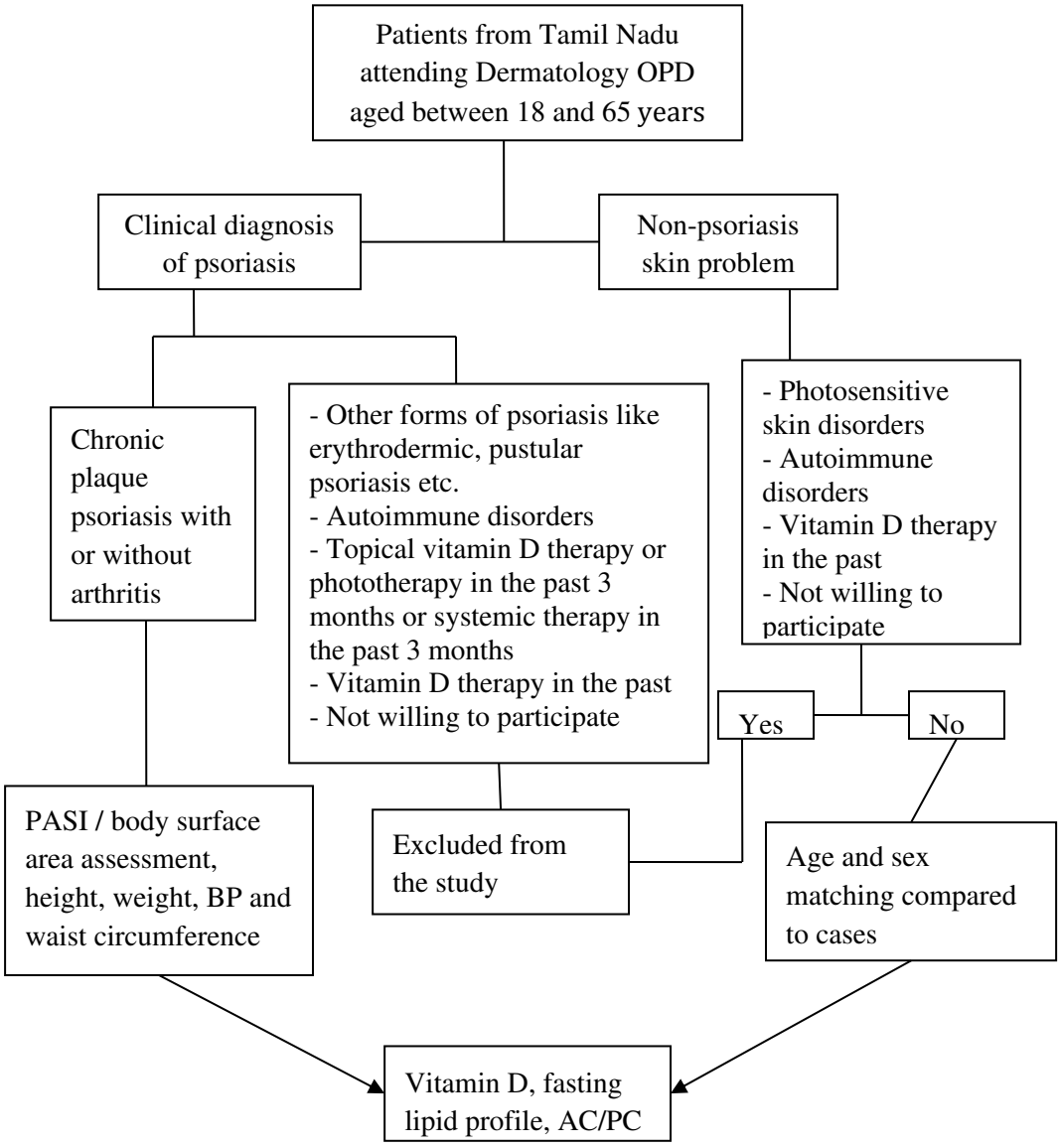


Figure 2 Algorithm showing the study methodology

Methodology:

The diagnosis of psoriasis was made based on the clinical features. All the patients, with psoriasis and controls with minor skin problems, who fulfilled the inclusion criteria, were enrolled into the study after obtaining informed consent. (Annexure – 1 & 2)

Age and sex matching was done between the subjects in patient and control group. Subjects of the same gender with age difference of ±2 years were considered as a matched pair.

The details pertaining to the study collected from the psoriasis patient group and from the control group was documented in separate clinical research proforma. (Annexure – 3 & 4)

Demographic details:

Demographic details regarding age and gender of the subjects, area of residence and occupation were recorded.

History pertaining to parameters likely to affect vitamin D:

1. Age of the subject – as reported by the subjects / as in Hospital records.

2. Gender

3. Residence - whether urban, semi-urban or rural.

4. Fitzpatrick skin type (76)

    - Always burn, never tan – skin type I

- Usually burn, tan less than average or with difficulty – skin type II

- Tans after initial burn – skin type III

- Burns minimally, tans easily – skin type IV

- Rarely burns, tans darkly easily – skin type V

- Never burns, always tans darkly – skin type VI

5. Occupation – Whether the occupation was indoor or outdoor was recorded. Those who were not employed were categorised under indoor if they spent less than 30 minutes per day for outdoor activities.

6. Average sun-exposure per day – The average sun-exposure per day in week days as well as in the weekends was documented and the average sun-exposure per week in hours was calculated.

7. Type of clothing - The study subjects were enquired on their clothing pattern while outdoor. They were categorised based on the area of photo-exposed skin as below:

    a. Minimal - if only face is photo-exposed (e.g. women wearing 'Burqa') or only face, hands and feet are photo-exposed (e.g. those wearing full sleeved shirts and full trousers)

    b. Moderate - if face, most of the upper limbs and feet are exposed. (e.g. Those wearing half sleeved shirts and trousers or saris)

c. Maximal - if face, upper limbs, most of trunk and most of lower limbs exposed (e.g. Agricultural field workers wearing only dhoti)

8. Sunscreen usage pattern – The subjects were enquired as to whether they used sunscreen and if they used, the frequency of usage and the sun protection factor (SPF) of the sunscreen were documented. The frequency of usage was categorised into 1 – Always, 2 – Mostly, 3- Occasional and 4 – Never.

9. Smoking – The subjects were enquired as to whether they smoked. If there was history of smoking, the pack years was calculated by multiplying the number of years of smoking by the number of packs of cigarettes smoked in a day. For example, one pack year = smoking 20 cigarettes (1 pack) per day x 1 year or 40 cigarettes /day for half a year.(77)

10. Alcohol intake – The subjects were enquired as to whether they consumed alcohol. If they consumed alcohol, the quantity of alcohol intake per week (in ml.) and the number of years of alcoholism was documented.

11. Average quantity of intake of fish and milk - Average quantity of vitamin D in non-fortified milk was taken as 40 IU in 1000ml.(78) The average vitamin D in 75g of fish was taken as 250 IU.(79)

History pertaining to psoriasis:

1. Age at onset of psoriasis as recollected by the patient when he or she noticed the first plaque was documented. The patients were categorised into type 1 or early onset psoriasis when the onset was before 40 years of age and type 2 when the onset was at or after 40 years of age.(26)
2. The disease duration was calculated and was categorised into < 1 year, 1 to 5 years and > 5 years.(45)
3. Data regarding any seasonal variation of the disease activity as observed by the patient.
4. Social avoidance – Patients were enquired if they avoided social activities. If they gave a positive response, then the reasons were categorised into 1 - social, 2 – disability, 3 – others.
5. Family history of psoriasis
6. Necessary information regarding past treatment was also collected.
7. Presence or absence of arthritis was documented.

Clinical examination:

1. The anthropometric measures such as height (cm) and weight (kg) were recorded.
2. The body mass index was calculated as weight (kg) divided by height (m) squared. Definitions for overweight and obesity were based on the WHO definitions for overweight and obesity in adults, that is BMI greater than or equal to 25 is overweight and greater than or equal to 30 is obesity. (80)
3. Waist circumference measurement was made (in cm) at the approximate midpoint between the lower margin of the last palpable rib and the top of the iliac crest.(81)

4. Blood pressure - Systolic and diastolic blood pressure (BP) were measured after a 5-minute rest and repeated again after a 10-minute interval. Average systolic and diastolic blood pressure was calculated.
5. The patient's skin, scalp and nails were examined and the details were recorded.
6. Psoriasis severity was documented in terms of body surface area involvement. In case of controls, the dermatological diagnosis and surface area of involvement were documented.
7. Joint examination was done and CASPAR (82) criterion, as below, was used for the diagnosis of psoriatic arthropathy. A minimal score of ≥ 3 was needed for making a diagnosis of psoriatic arthropathy.

1	Skin psoriasis Present - Past -	 2 1
	Family history, if patient not affected	1
2	Nail (pits / onycholysis / hyperkeratosis)	1
3	Dactylitis	1
4	Rheumatoid factor negative	1
5	Juxtaarticular new bone formation	1

8. The type of arthritis was classified based on the Moll and Wright's classification (82) as given below:
    a. symmetric polyarthritis resembling rheumatoid arthritis
    b. asymmetric oligoarthritis
    c. arthritis mutilans
    d. spondyloarthritis
    e. distal interphalangeal predominant

9. Nail involvement was documented and NAPSI (Annexure – 3) score was calculated.

Severity of psoriasis:

The extent of the disease was measured by the body surface area (BSA) involved according to Wallace's formula of 9 in adults.(83) The disease severity was classified into mild, moderate and severe, if the percentage of BSA involved was < 3%, 3-10% and > 10% respectively.(84)

The PASI scoring (Annexure – 3) was done for chronic plaque psoriasis as a measure of clinical severity. The score ranges from 0-72 representing no involvement to complete involvement (erythroderma) of the severe possible degree.

The severity of psoriasis was graded, based on PASI score into mild (< 7), moderate (7 - 12) and severe if the PASI score was >12.(85)

Laboratory parameters:

1. Vitamin D level (25-hydroxyvitamin D) was measured for all the patients and controls. It was considered normal if the value was ≥ 30 ng/ml, deficient – if ≤ 20 ng/ml and insufficient if between 20 -30 ng/ml.(64) Serum 25-OH vitamin level was determined by chemiluminescence method in the clinical biochemistry department of our hospital.
2. Fasting blood sugar and 2 hour post prandial blood sugar were measured for all subjects.
3. Fasting lipid profile was measured for all subjects.
4. The diagnosis of metabolic syndrome was made based on the criteria proposed by the new International Diabetes federation. (Annexure - 5)(44) Central obesity was taken as

the essential criteria. Ethnicity specific waist circumference cut-off for central obesity as recommended for Indians i.e. ≥ 90 cm for men and ≥ 80 cm for women was used. Of those who were noted to have central obesity, if they fulfilled any two of the four below mentioned criteria, they were diagnosed to have metabolic syndrome.

- Systolic BP ≥ 130 mmHg or diastolic BP ≥ 85 mmHg or known hypertensives on treatment
- Raised triglyceride levels(≥150 mg/dl) or on treatment for dyslipidemia
- Low HDL cholesterol level for their gender (< 40mg/dl for males and < 50mg/dl for females) or on treatment for dyslipidemia
- Elevated fasting blood sugar level (≥ 100 g/dl) or known diabetics on treatment

5. In patients with active arthropathy, C-reactive protein, Rheumatoid factor and joint X – ray were done.

Sample size:

The sample size of the study was calculated as explained below:

For 5% error and 80% power, the sample size required would be

$$n = \frac{7.84 \times [p1\,(1-p1) + p2\,(1-p2)]}{(p1 - p2)^2}$$

p1 - prevalence of vitamin D deficiency in the control group

p2 - prevalence of vitamin D deficiency in the psoriasis group

The sample size was calculated based on an Italian study published by Gisondi et al.,(13) as there were no published Indian studies on the prevalence of vitamin D deficiency in patients with psoriasis when this study was planned.

Based on the previous study -

p1 was taken as 29.7% (30%)

p2 was taken as 57.8% (58%)

$$n = \frac{7.84 \times [0.3\,(1 - 0.3) + 0.58\,(1 - 0.58)]}{(0.3 - 0.58)^2}$$

$$= 45.3$$

$$= 45$$

Therefore a minimum of 45 patients were required in each arm.

In India, the prevalence of vitamin D deficiency is high (73,74) and it could be a limitation of this study. However due to financial constraints, this was planned as a pilot study to help us in further planning of larger trials.

Statistical methods:

Data were entered in EpiData version 3.1, and analysed using the software STATA version 13.0. Continuous variables were summarised using mean and standard deviations and categorical variables were summarised using frequencies along with percentages. The t–test was used to check the group mean differences. Chi square test was used to check the association

between categorical variables. Conditional logistic regression was performed taking the vitamin D deficiency and disease status as outcome. Univariate analysis was done to check the impact of predictors. A linear regression was performed having the log transformed vitamin D levels as outcome. Skewed variables were log transformed and back transformed and interpreted as percentage change. A multivariate analysis was performed adjusting for skin type, occupation, locality and metabolic syndrome with the important predictors.

Study approval:

This study was approved by the Institutional Review Board. (IRB No - 8593[observe])

Results

During the study period (December 2013 to August 2014), there were 352 patients who were diagnosed to have psoriasis. Of those 352 patients, 53 patients with chronic plaque psoriasis who fulfilled the inclusion criteria and willing for the study were recruited, after obtaining informed consent. Forty-seven patients with non-psoriatic, non-photosensitive minor dermatological ailments fulfilling the inclusion criteria for controls were recruited after obtaining informed consent.

A total of 100 subjects (53 patients and 47 controls) were recruited into the study. Of the 53 patients, only 45 had given blood sample for vitamin D testing. Age and sex matching was done only for those 45 patients whose vitamin D results were available. Hence finally there were 45 cases and 45 age and sex matched controls. These 45 cases and 45 age and sex matched controls were taken for the final analysis (Annexure - 6).

The flow chart (figure 3) shows patient recruitment process followed in our study.

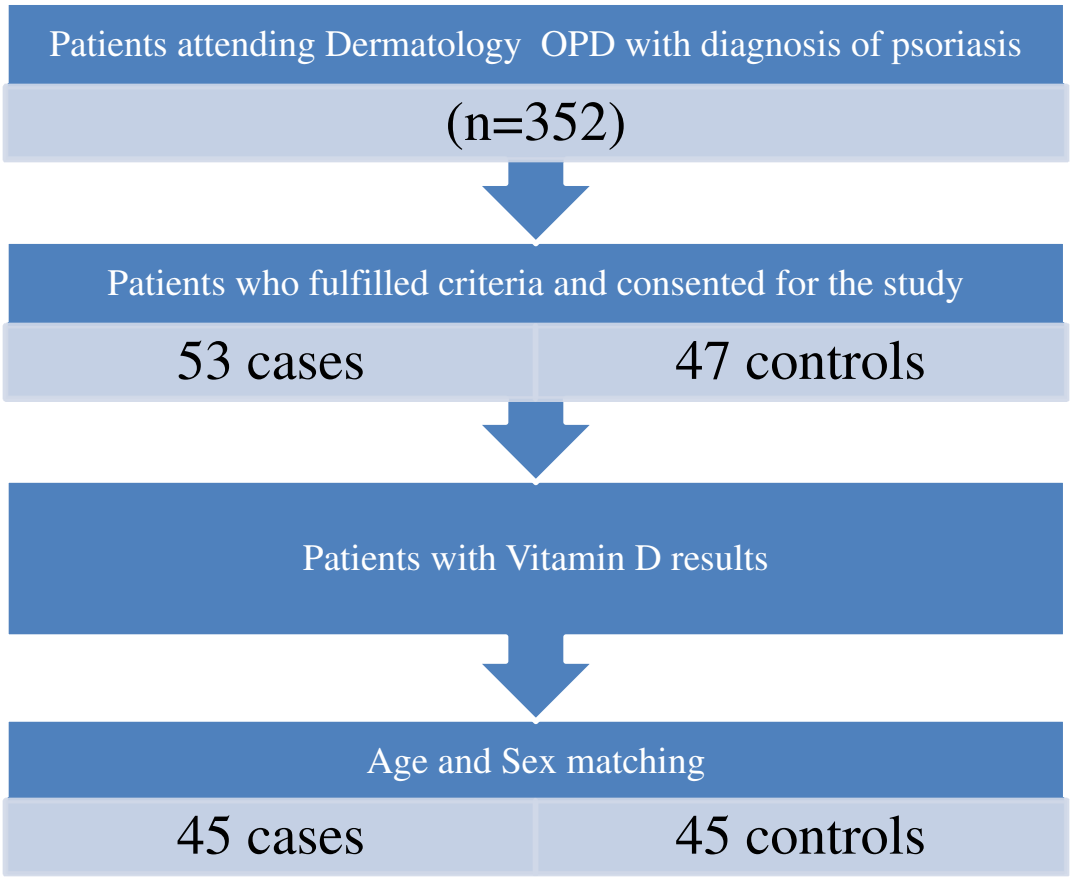


Figure 3: Flowchart showing the protocol followed for patient recruitment

1. Baseline characteristics

1.1. Age and gender distribution

The age of the subjects ranged from 18 years to 65 years. The mean age of the cases was 41.62 years (± 37.92). The mean age of the control group was 41.29 years (± 37.56).

There were 26 males (57.78%) and 19 females (42.22%) in both the study groups (figure 4). Since matching was done, there was no difference between both the groups with respect to age and gender distribution (p = 0.90 for age and p = 1 for gender). The male: female ratio in our study group was 1.38: 1.

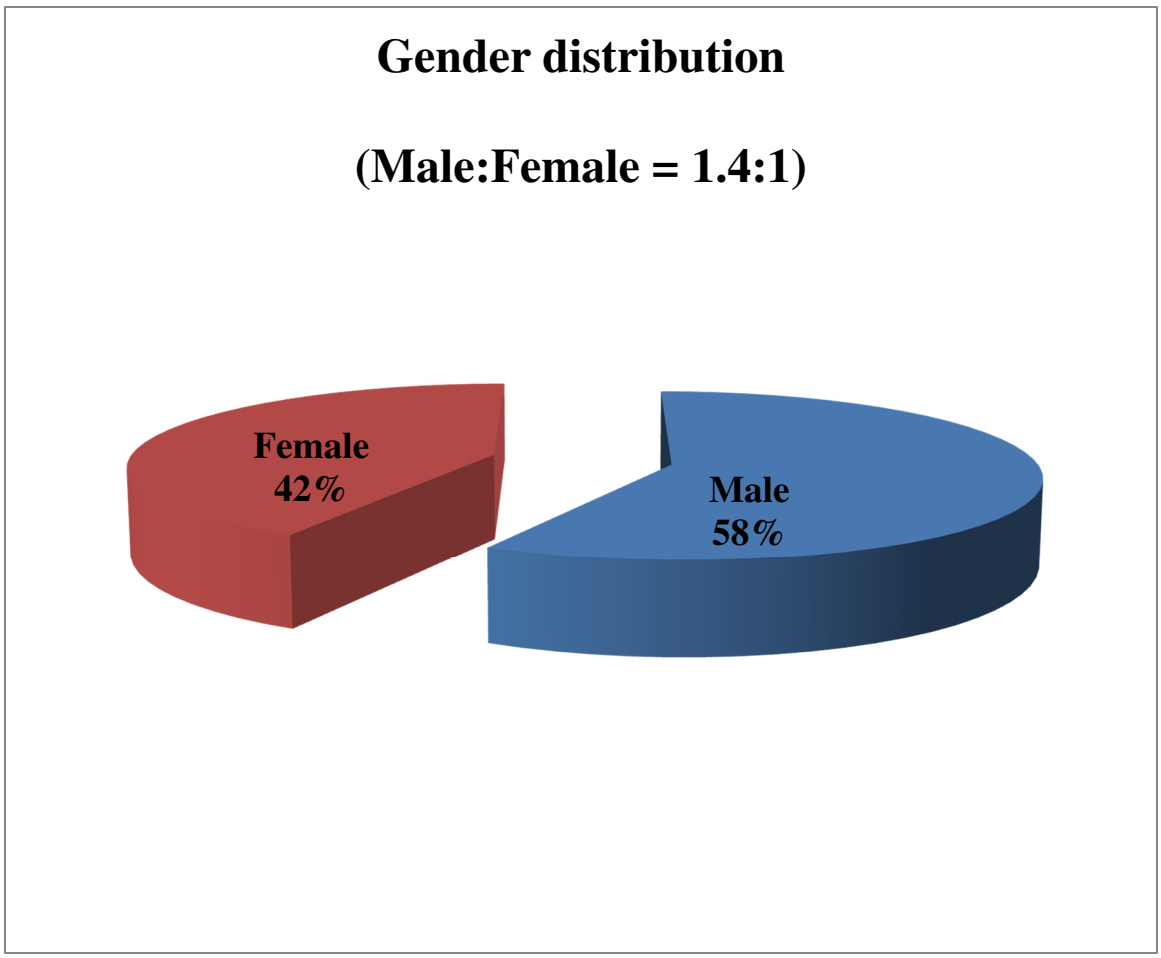
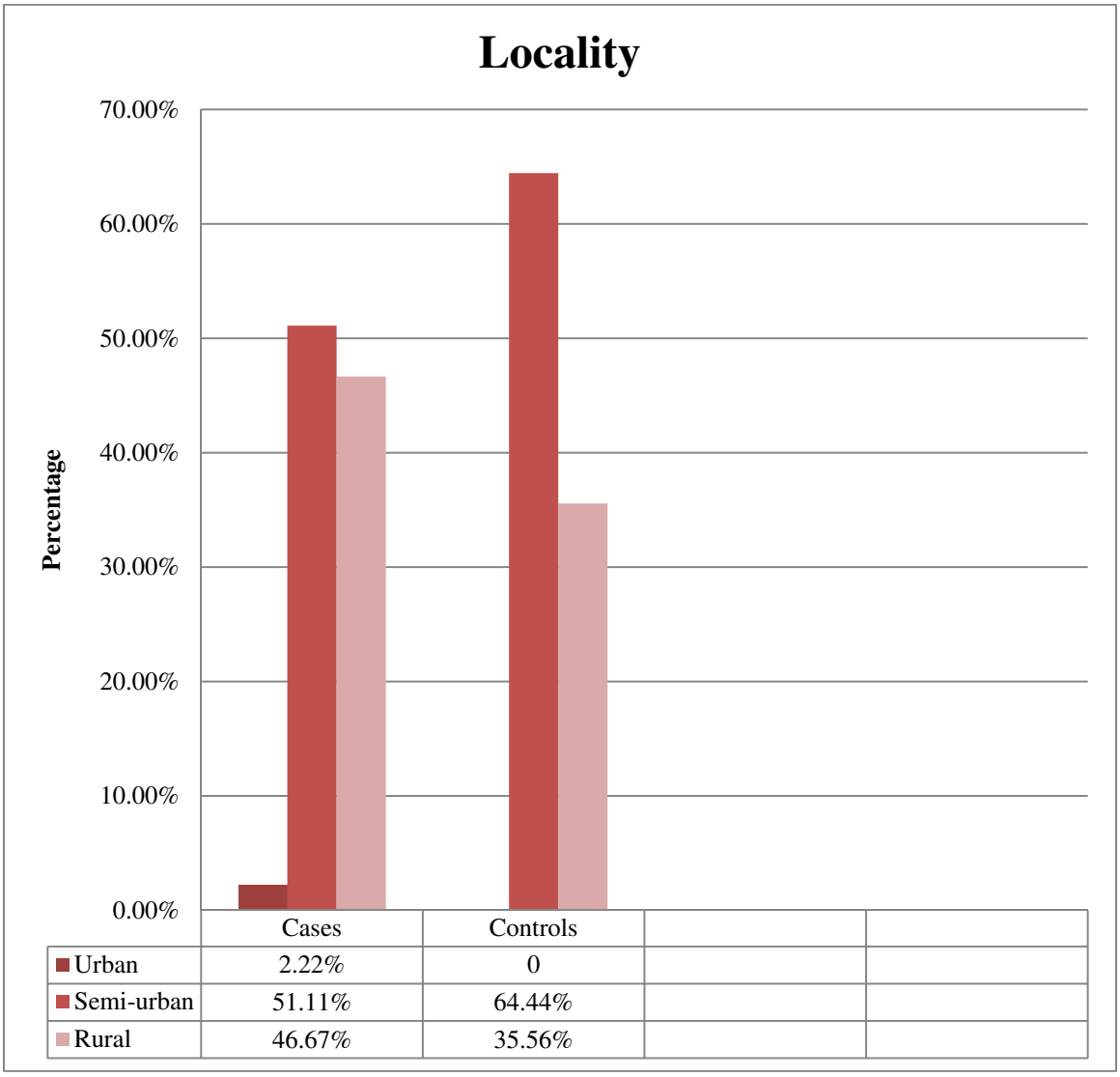


Figure 4: Gender distribution of the study subjects

1.2. Locality and occupation distribution

Majority of our study subjects (57.78%) were from semi-urban areas. There was only one individual from urban set up (1.11%) and 37 (41.11%) were from rural set up. Among the cases, there were 21 (46.67%), 23 (51.11%) and 1 (1.11%), from rural, semi-urban and urban set up respectively. Among the controls there were 16 (35.56%) and 29 (64.44%) from rural and semi-urban setup respectively. There was no statistical difference between the patients and controls in

relation to the locality (p=0.31). Figure 5 shows the distribution of cases and controls based on locality.



	Cases	Controls		
Urban	2.22%	0		
Semi-urban	51.11%	64.44%		
Rural	46.67%	35.56%		

Figure 5: Distribution of study population based on locality

Nineteen (42.22%) in each arm were engaged in outdoor occupation and 26 (57.78%) in each arm were engaged in indoor activities. Though matching with respect to occupation was not intentionally done, both the arms had exactly the same number of subjects working indoors and outdoors, as shown in figure 6.

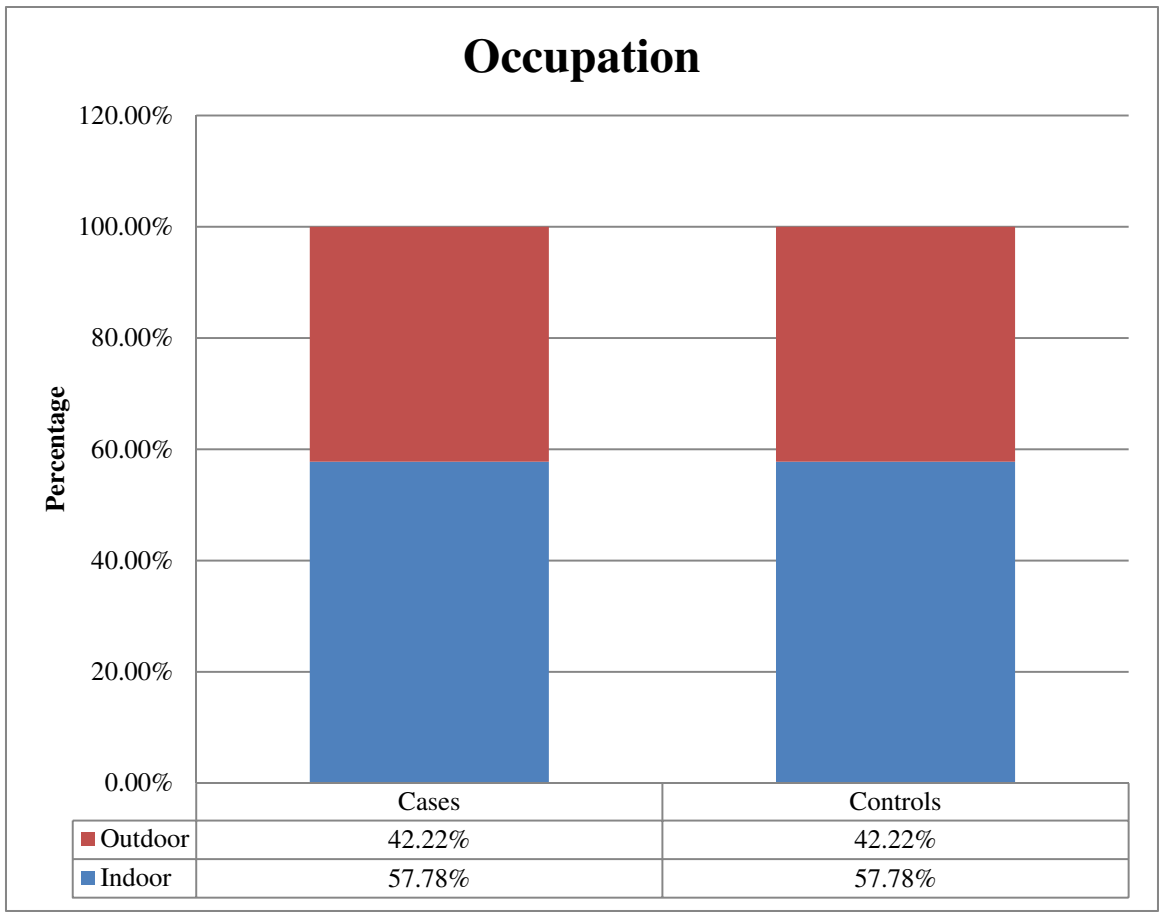


Figure 6: Type of occupation among the study subjects

1.3. Skin type and type of clothing

The study subjects had either Fitzpatrick skin type IV or V. Fitzpatrick type IV skin was observed in 10 (22.2%) subjects and Fitzpatrick type V skin was observed in 35 (77.78%) subjects in each arm.

The clothing pattern of the subjects were categorised into minimal, moderate and maximal based on the amount of photo-exposed skin as explained in the methodology section. Since there were only 6 subjects in the 'maximal' category, they were clubbed with the 'moderate'

group during analysis. Among the cases there were 14 (31.11%) patients under the minimal photo-exposed category and 31 (68.89%) patients under the moderate category. Among the controls, there were 5 (11.11%) subjects under the minimal photo-exposed category and 40 (88.89%) subjects under the moderate photo-exposed category (figure 7). This difference was found to be statistically significant (p = 0.02). Many psoriasis patients reported of wearing more covered type of clothing to avoid social stigma when they had lesions in the exposed parts.

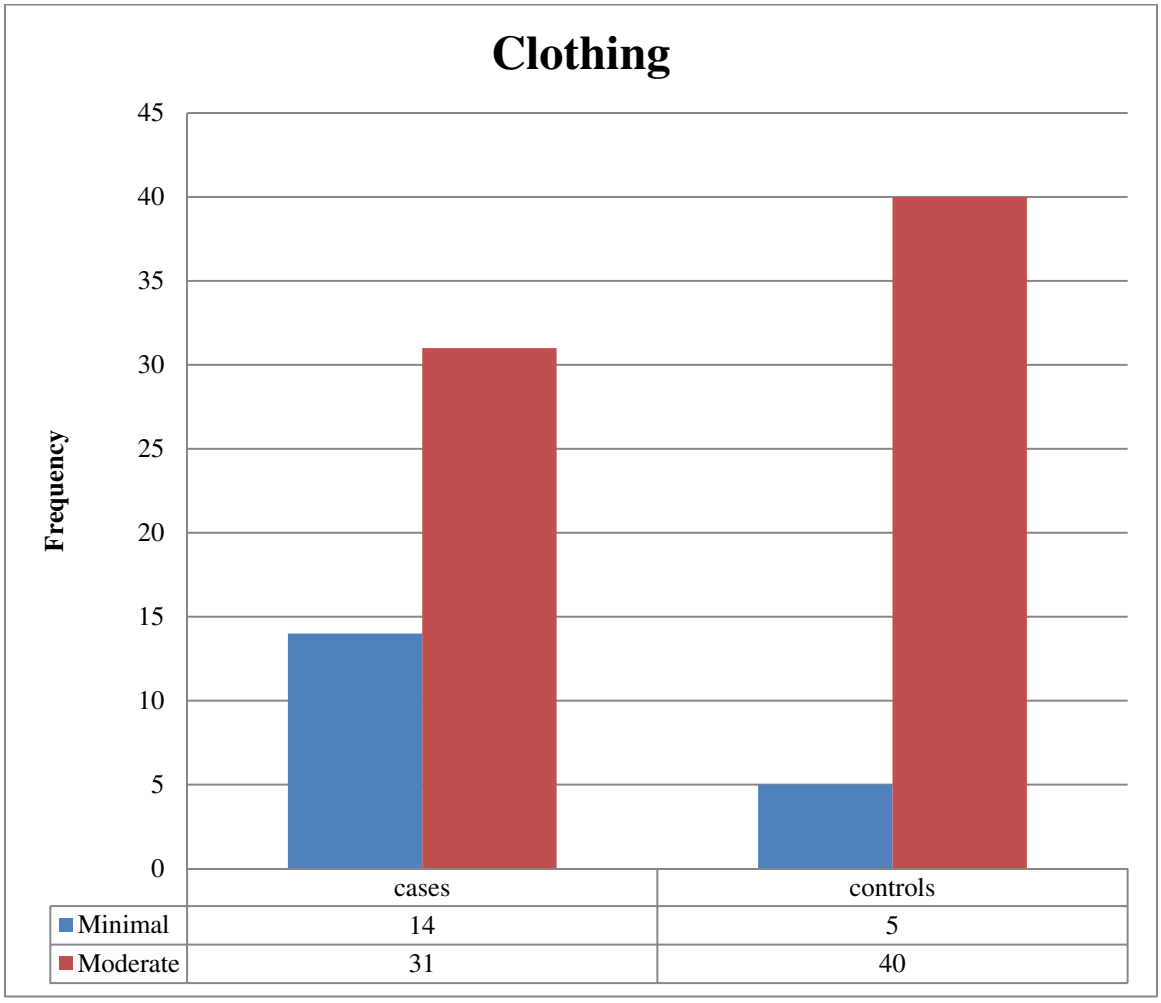


Figure 7: Type of clothing among the study subjects

(Note: Minimal – less photo-exposed; Moderate – Moderately photo-exposed)

1.4. Sun-exposure and sunscreen usage

The hours of sun-exposure per week among the cases ranged from 1 hour 35 minutes to 56 hours and among the controls it ranged from 1 hour 10 minutes to 56 hours (p = 0.61). Eighteen (40%) cases had less than or equal to 30 minutes of average sun-exposure per day which was taken as inadequate sun-exposure and 20 (44.44%) controls had less than or equal to 30 minutes of average sun-exposure per day.

There were only four (4.44%) sunscreen users in the study group, all of whom belonged to the control arm. Among the sunscreen users, only one person (1%) used sunscreen regularly. Since the usage of sunscreen was very occasional in the other three subjects, further analysis was not done on this parameter.

Table 5 shows the baseline characteristics of the study population.

Table 5 – Baseline characteristics of the study population:

Variable	Cases *n=45*	Controls *n=45*	*p*-value
Age (years) mean ± SD	41.62 ± 12.33	41.29 ± 12.40	0.90
Sex [Frequency(%)]			1.00
Male	26 (57.78)	26 (57.78)	
Female	19 (42.22)	19 (42.22)	
Locality [Frequency(%)]			0.31
Urban	1 (2.22)	0 (0.00)	
Semi-urban	23 (51.11)	29 (64.44)	
Rural	21 (46.67)	16 (35.56)	
Occupation [Frequency(%)]			1.00
Indoor	26 (57.78)	26 (57.78)	
Outdoor	19 (42.22)	19 (42.22)	
Fitzpatrick Skin type [Frequency(%)]			1.00
IV	10 (22.22)	10 (22.22)	
V	35 (77.78)	35 (77.78)	
Clothing based on photoexposed skin.[Freq (%)]			**0.02**
Minimal	14 (31.11)	5 (11.11)	
Moderate	31 (68.89)	40 (88.89)	
Sun-exposure			
Avg. hours /week [median(min, max)]	7(1.35,56)	7(1.10,56)	0.61
Avg hours/day < 30 min. [Freq (%)]	18 (40)	20 (44.44)	0.67

SD – Standard deviation; Avg – Average; min – minimum; max – maximum; Freq - frequency

2. Behavioural patterns of study subjects

2.1. Smoking

There were a total of 9 (10%) smokers among the study subjects. The pack years ranged from 0.5 to 25. Among the 9 smokers, 6 belonged to the control group and 3 belonged to the cases. 6.67% of the patients and 13.33% of the controls were smokers (figure 8). There was no statistical difference ($p = 0.29$) with respect to smoking between both the groups.

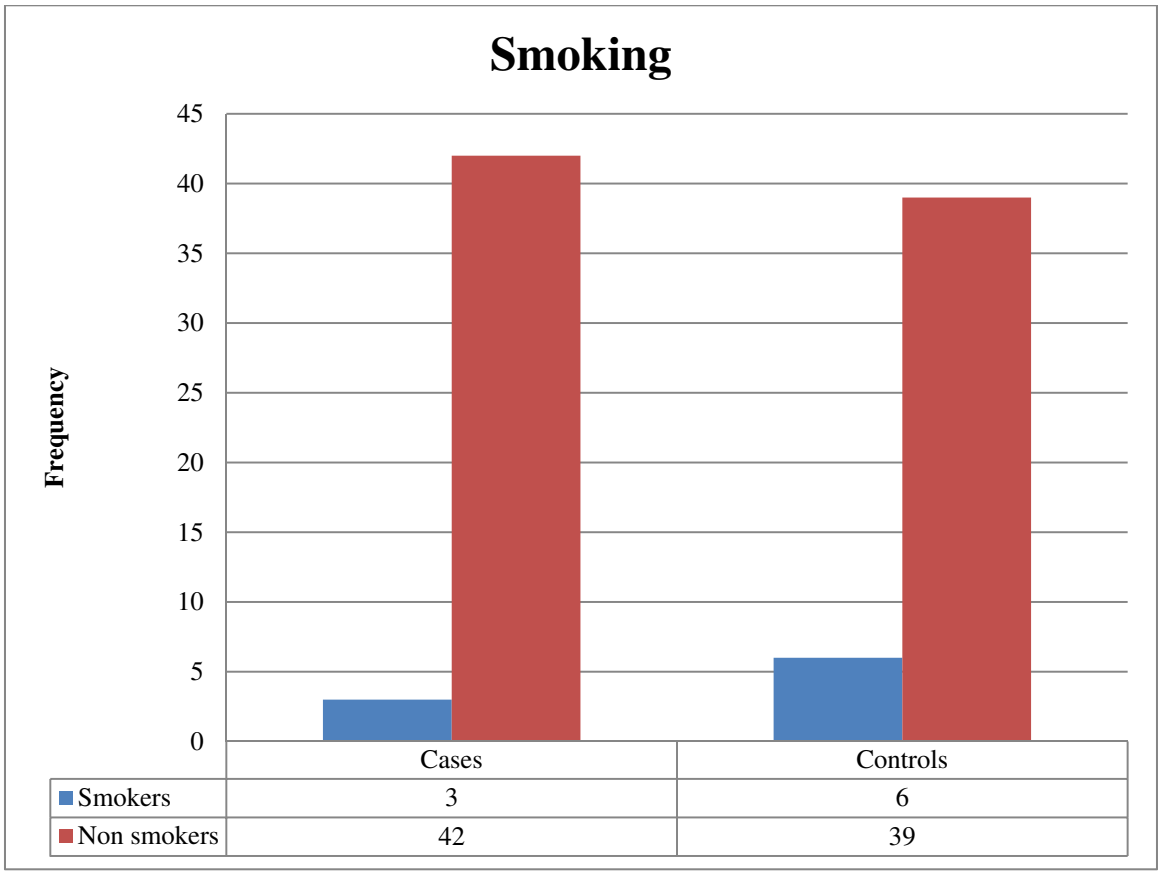


Figure 8 – Smoking among the study subjects

2.2. Alcohol consumption

Among the cases, there were 7 (15.56%) subjects who consumed alcohol whereas among controls there were only 2 (4.44%) subjects who consumed alcohol. However, this difference was not statistically different (p = 0.079). In the control group, the average (minimal, maximal) monthly consumption of alcohol was 240 ml/month (120 ml, 360 ml) and that in cases was 545 ml/month (20 ml, 2520 ml).

2.3. Oral intake of vitamin D in the form of dairy products and fish

The oral vitamin D intake in the form of dairy products and fish was found to be very low in our study subjects. Among cases it ranged from 0 IU to 302 IU with a median of 16 IU. Among controls, it ranged from 2 IU to 101 IU with a median of 18 IU. Table 6 shows the behavioural patterns of the study population.

Table 6 – Behavioural pattern of the study subjects:

Variable	Cases *n=45*	Controls *n=45*	*p*-value
Smoking [Frequency (%)]			0.29
Yes	3 (6.67)	6 (13.33)	
No	42 (93.33)	39 (36.67)	
Alcohol intake [Frequency (%)]			0.079
Yes	7 (15.56)	2 (4.44)	
No	38 (84.44)	43 (95.56)	
Dietary vitamin D IU/day [Median(min, max)]	16 (0, 302)	18 (2, 101)	0.62

IU – International units; min – minimum; max - maximum

3. Known co-morbidities in the study group

3.1. Diabetes Mellitus

Ten (22.22%) cases and 7 (15.56%) controls were known diabetics on treatment. There was no significant difference (p = 0.419) in the distribution of known diabetics among the groups. Figure 9 shows the known co-morbidities among the study subjects.

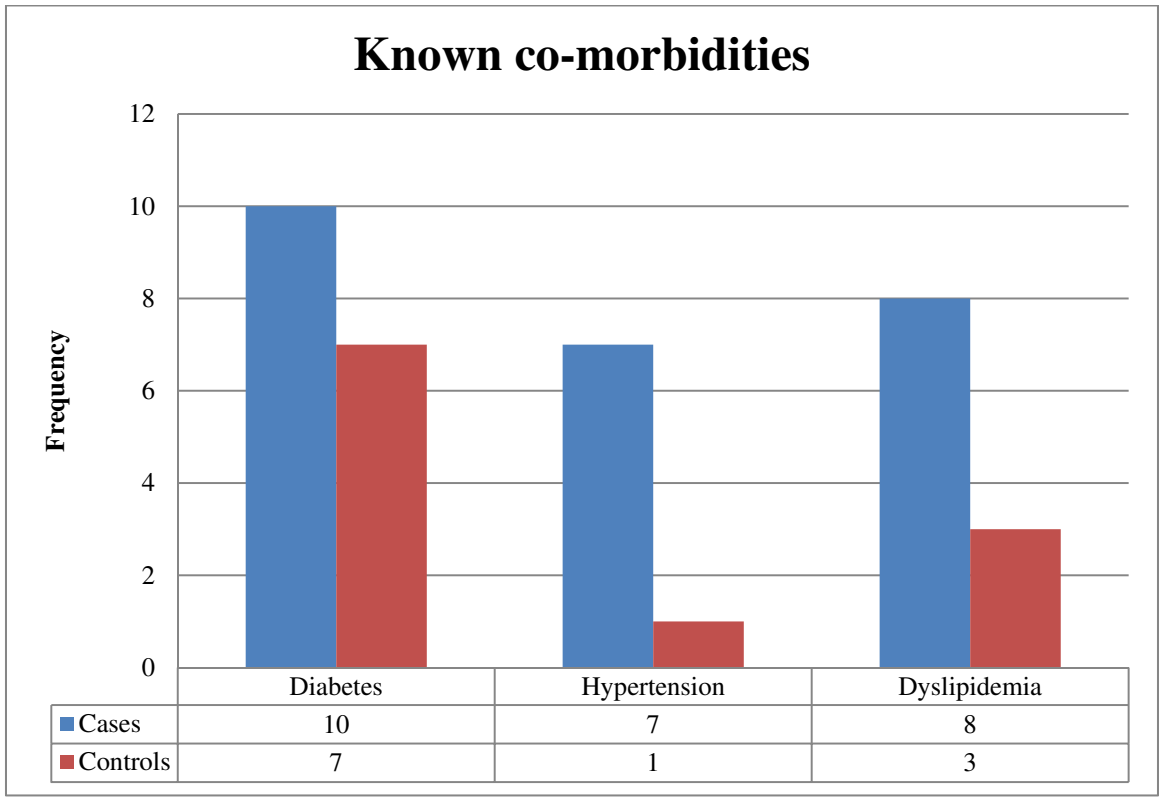


Figure 9: Known co-morbidities among the study group

3.2. Hypertension

Seven (15.56%) cases and 1 (2.22%) control subject were known hypertensives. This distribution was found to be statistically significant (p = 0.026).

3.3. Dyslipidemia

Eight (17.78%) patients with psoriasis were known cases of dyslipidemia. But among controls there were only 3 (6.67%) subjects with dyslipidemia. However, this difference was not found to be statistically significant (p = 0.108). Table 7 shows the known co-morbidities among the study subjects.

Table 7 – Known co-morbidities in the study population

Variable	Cases *n=45*	Controls *n=45*	*p*-value
Diabetes Mellitus [Frequency (%)]			0.419
Yes	10 (22.22)	7 (15.56)	
No	35 (77.78)	38 (84.44)	
Hypertension [Frequency (%)]			**0.026**
Yes	7 (15.56)	1 (2.22)	
No	38 (84.44)	44 (97.78)	
Dyslipidemia [Frequency (%)]			0.108
Yes	8 (17.78)	3 (6.67)	
No	37 (82.22)	42 (93.33)	

4. Metabolic syndrome related parameters

4.1. Body Mass Index (BMI) and abdominal obesity

Fifteen (33.33%) cases had a body mass index less than 25, whereas, among the controls, twenty nine (64.44%) had body mass index less than 25. Seventeen (37.78%) cases and 8 (17.78%) controls were overweight (BMI between 25 and 30). Thirteen (28.89%) cases and 8 controls (17.78%) were obese (BMI more than 30). The cases had a 4.75 times more risk of being overweight and 4.17 times more risk of being obese as compared to the controls. These variations in BMI were found to be statistically significant [$p = 0.011$ (overweight) and $p = 0.028$ (obesity)]. The mean BMI among the cases was 27.12 ± 5.68 and that of the controls was 24.68 ± 4.82 ($p = 0.03$). Figure 10 shows the categorisation of subjects based on BMI.

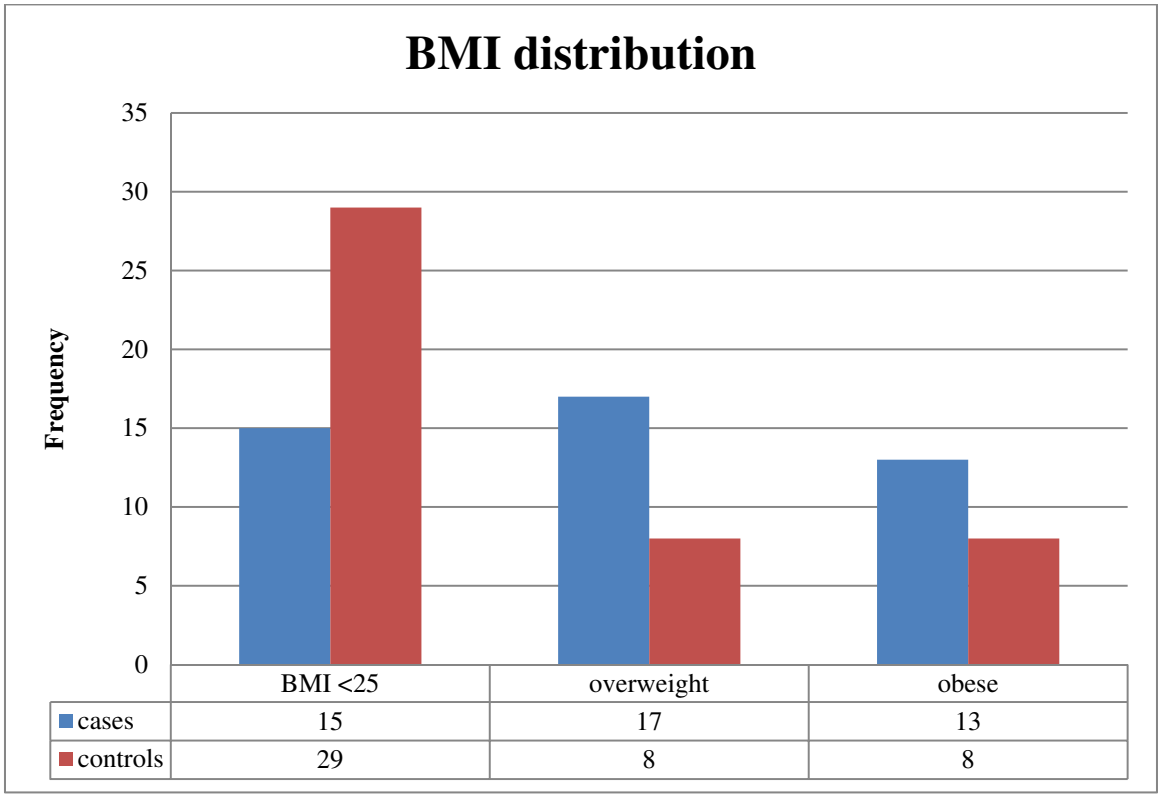


Figure 10: Categorisation of the study groups based on body mass index

Abdominal obesity as defined (for Indian ethnicity) as waist circumference ≥ 90 cm in men and ≥ 80 cm in women was present in 31 (68.89%) cases and 19 (42.22%) controls (figure 11). The patients with psoriasis were found to have 3.4 times higher risk for central obesity. This difference was found to be statistically significant (odds ratio 3.4, 95% confidence interval 1.25 – 9.22, $p = 0.016$). The mean waist circumference among cases was 91.33 ± 13.18 cm and that of the controls was 84.49 ± 11.59 cm ($p = 0.01$).

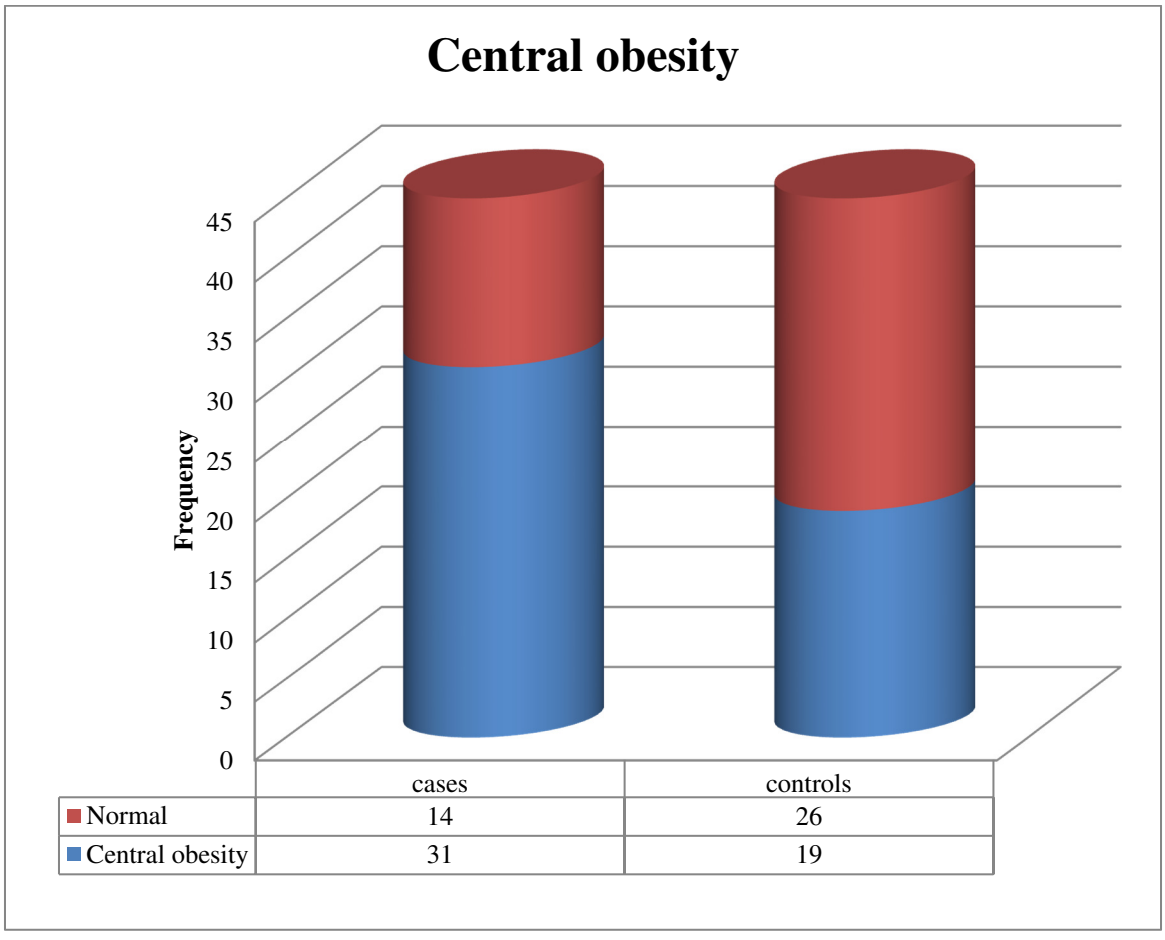


Figure 11: Central obesity among the study groups

4.2. Raised fasting glucose level

Nineteen (42.2%) cases and 15(33.4%) controls had either elevated fasting blood sugar level (≥ 100 g/dl) or were known diabetics on treatment. The patients with psoriasis had 1.6 times higher risk of having raised fasting glucose level as compared to controls [Odds ratio 1.6, 95% confidence interval (0.60 - 4.053)]. This difference was not found to be statistically significant ($p = 0.35$).

4.3. Raised blood pressure

Twenty four (53.33%) cases and 7 (15.56%) controls had high blood pressure as suggested by the International Diabetes Federation which is systolic BP ≥ 130 mmHg or diastolic BP ≥85 mmHg or known hypertensives on treatment. This difference was found to be statistically significant ($p = 0.002$). Psoriatic patients were at a 9.5 times higher risk of having raised blood pressure as compared to the controls. (Confidence interval 2.1 – 40.8)

The mean systolic blood pressure was 132 ± 17 mmHg and 120 ± 13 mmHg among the cases and controls respectively ($p < 0.001$). The mean diastolic blood pressure was 85 ± 12 mmHg and 78 ± 8 mmHg among the cases and controls respectively ($p = 0.001$).

4.4. Raised triglycerides

Fifteen (33.33%) cases and 12 (26.67%) controls had raised triglyceride levels (≥150 mg/dl) or were already on treatment for dyslipidemia. This difference was not found to be statistically significant ($p = 0.69$). The mean triglyceride level was 139 ± 88 mg/dl and 115 ± 63 mg/dl among the cases and controls respectively ($p = 0.10$).

4.5. Reduced HDL cholesterol

Thirty (66.67%) of the cases and 27 (60%) of the controls had low HDL cholesterol level for their gender (< 40mg/dl for males and < 50mg/dl for females) or were already on treatment for dyslipidemia. This difference was not found to be statistically significant (p = 0.69). The mean HDL cholesterol level was 41 ± 9 mg/dl and 40 ± 10 mg/dl among the cases and controls respectively (p = 0.68).

Figure 11 shows the distribution of metabolic syndrome related parameters among the subjects.

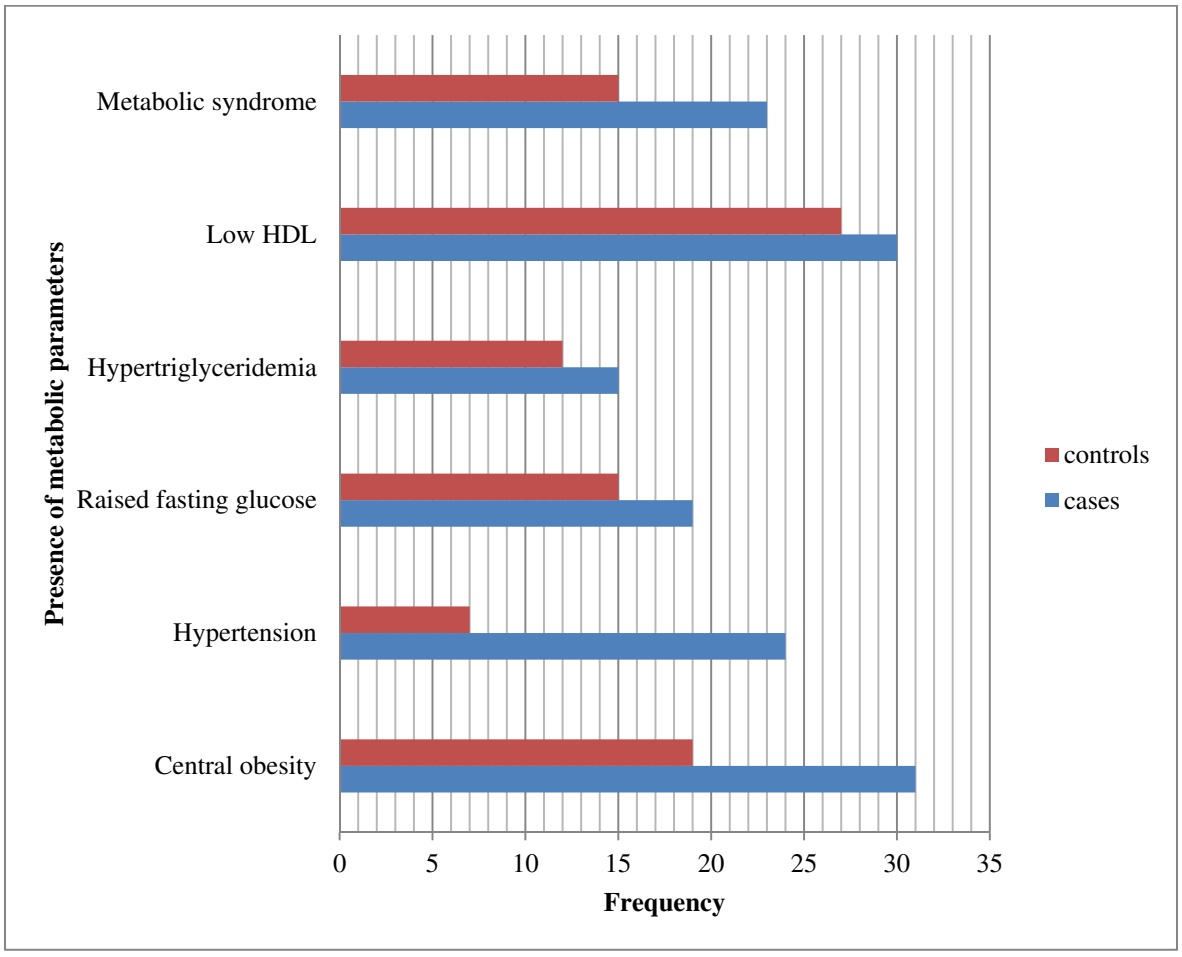


Figure 12: Metabolic syndrome related parameters among the study groups

4.6. Metabolic syndrome

Alarmingly, 38 (42.22%) of our study subjects fulfilled the criteria for metabolic syndrome as put forth by the International Diabetes Federation. Twenty three (60.5%) of them were patients with psoriasis.

Twenty three (51.1%) of the 45 psoriatic patients and 15(33.33%) of the controls were found to have metabolic syndrome. Patients with psoriasis had a 2.3 times higher risk of metabolic syndrome as compared to the controls though it did not reach a level of statistical significance ($p = 0.08$). Table 8 shows the distribution of metabolic syndrome related parameters among the study subjects.

Table 8 – Metabolic syndrome related parameters

Variable [Frequency (%)]	Cases *n=45*	Controls *n=45*	Odds ratio (95% Confidence interval)	*p*-value
Central obesity	31 (68.89)	19(42.22)	3.4(1.25 – 9.22)	**0.02**
Hypertension	24(53.33)	7 (15.56)	9.5(2.1 – 40.8)	**0.002**
Raised fasting glucose	19 (42.2)	15(33.4)	1.6(0.60 - 4.053)	0.35
Hypertriglyceridemia	15 (33.33)	12 (26.67)	1.38(0.56 – 3.41)	0.69
Low HDL	30 (66.67)	27 (60.0)	1.38(0.56 – 3.41)	0.69
Metabolic syndrome	23 (51.1)	15(33.33)	2.33(0.9 – 6.7)	0.08

5. Psoriasis patient profile

5.1. Age at onset and duration of psoriasis vulgaris

The age at onset of psoriasis in our study group ranged from 5 years to 60 years. The mean age at onset of the disease was 31.24 years. The duration of psoriasis at the time of recruitment into the study ranged from 3 months to 52 years. The mean duration of the disease was 10.38 years and the median was 6 years.

Four (8.89%) patients had disease duration less than 1 year, 18 (40%) patients had disease duration ranging between 1 and 5years and 23(51.11%) patients had the disease for more than 5 years. The presence or absence of metabolic syndrome did not correlate (p = 0.74) with the disease duration as shown in the table 9.

Table 9 – Correlation of disease duration with metabolic syndrome

Disease duration	Metabolic syndrome Present [Frequency (%)]	Metabolic syndrome Absent [Frequency (%)]	Total [Frequency (%)]
< 1 year	2(9.09)	2(8.70)	4(8.89)
1 to 5 years	10 (45.45)	8 (34.78)	18 (40)
> 5 years	10(45.45)	13(56.32)	23(51.11)
Total	22(100)	23(100)	45(100)

5.2. Type 1 and type 2 psoriasis

Thirty three (73.33%) patients had early onset or type 1 psoriasis (onset before 40 years of age) and 12 (26.7%) patients had type 2 psoriasis. Three patients with type 1 disease and 2 patients with type 2 disease had a positive family history. Among those with type 1 psoriasis, 14 (42.42%) of them had metabolic syndrome and among those with type 2 psoriasis, 9 (75%) had metabolic syndrome (p = 0.053). Figure 13 shows the distribution of metabolic syndrome among patients with type 1 and type 2 psoriasis.

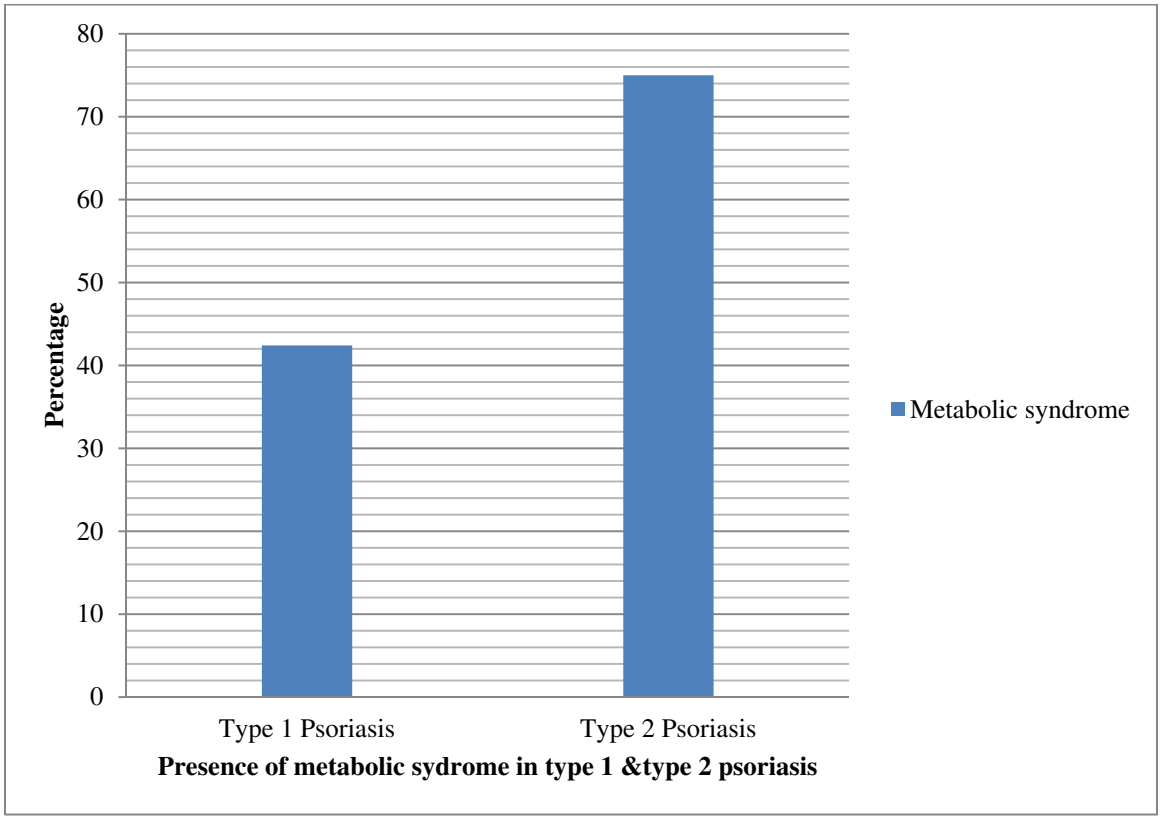


Fig 13: Metabolic syndrome in type 1 and type 2 psoriasis

5.3. Seasonal variation

Of the 45 patients with psoriasis, 18 (40%) patients had winter exacerbation and 6 (13.33%) patients had summer exacerbation. The remaining 21 (46.67%) patients had not observed any seasonal variation in the disease activity.

5.4. Family history

Five (11.11%) of the patients gave a positive family history of psoriasis. Three of these patients had type 1 psoriasis and two of them had type 2 psoriasis ($p = 0.48$). None of the control group subjects had family members having psoriasis.

5.5. Social avoidance

Fourteen (31.11%) patients avoided social activities due to the presence of the disease. All of them attributed the avoidance to social reasons.

5.6. Disease severity measures - Body surface area involvement and PASI

The body surface area (BSA) involvement among the patients ranged from 2% to 50%. Only one person (2.22%) had BSA involvement of less than 3%. Seven (15.56%) individuals had BSA involvement more than 10%. Thirty seven (82.22%) patients had BSA involvement between 3 and 10 per cent.

Figure 14 shows the categorisation of disease severity based on BSA among the cases.

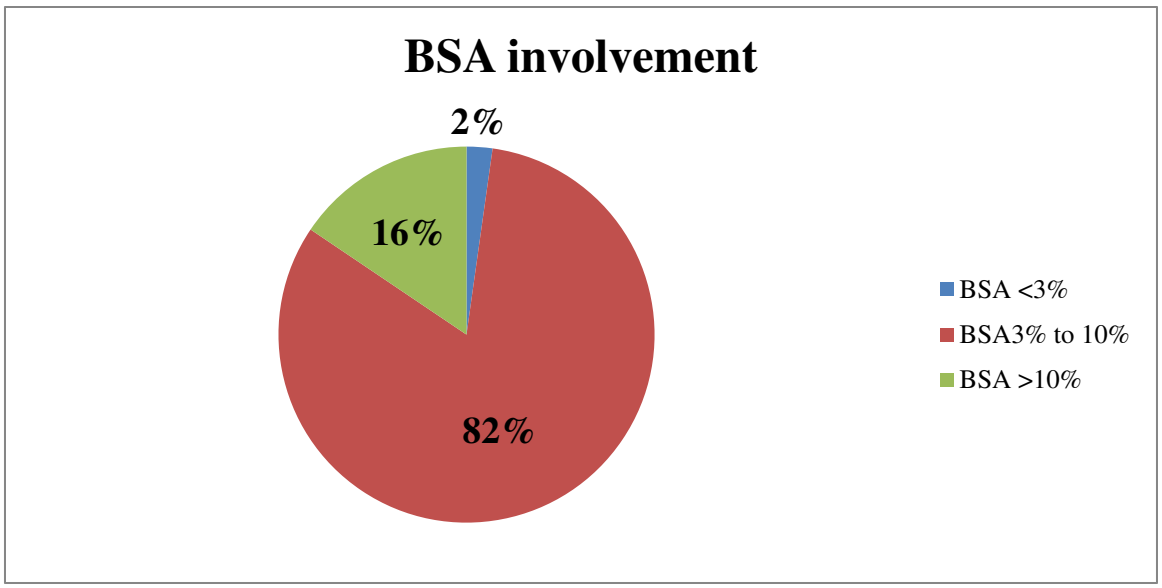


Figure 14: Body surface area involvement among the patients

Majority of the patients, 35 (77.78%), had a PASI score less than 7. Seven (15.56%) patients' PASI score ranged between 7 & 12 and 3 (6.67%) patients' PASI score was above 12 (figure 15). The mean PASI score was 5.27 ± 3.61.

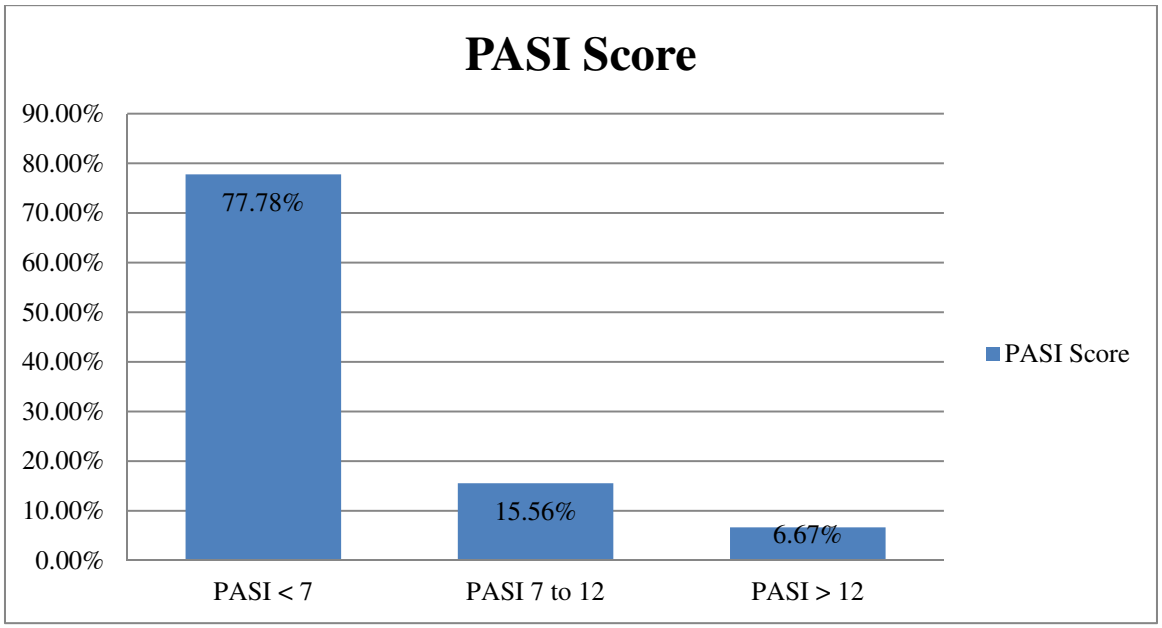


Figure 15: PASI score of the patients

There was no correlation of PASI (r = -0.236, p = 0.12) as well as BSA involvement (r = -0.224, p = 0.14) with the BMI of the patients.

5.7. Psoriatic arthritis

Five (11.11%) of the 45 patients had psoriatic arthritis, out of which three had symmetrical polyarthritis and one each had asymmetric oligoarthritis and spondyloarthritis. All the 5 patients with arthropathy met the CASPAR criteria for psoriatic arthritis. The CRP level was elevated in 4 of them. The CRP level ranged from 1.48 to 49.7 mg/ l and the median value was 30 mg/l.

5.8. Nail involvement and NAPSI

Two third (67.67%) of the 45 patients with psoriasis were noted to have psoriasis related nail changes, the commonest change being pits. The NAPSI score among our patients ranged from 0 to 37.

6. Control patient profile

In the control arm, we had patients who presented with minor skin complaints like warts, fissures over the heels, superficial fungal infection etc. The frequency of each of the dermatological diagnosis is shown in table 10. The body surface area of involvement in all the cases were less than or equal to 5%.

Table 10 – Dermatological diagnosis among the control group

Sl. No.	Dermatological diagnosis	Frequency (%)
1	Superficial fungal infection	9 (20%)
2	Viral wart	5 (11.11%)
3	STI screening	1 (2.22%)
4	Herpes labialis	1 (2.22%)
5	Molluscum contagiosum	1 (2.22%)
6	Pityriasis capitis	2 (4.44%)
7	Fissures over heels	5 (11.11%)
8	Erythrasma	4 (8.89%)
9	Cherry angioma	2 (4.44%)
10	Keloid	2 (4.44%)
11	Zoons balanitis	1 (2.22%)
12	Acne grade 1	2 (4.44%)
13	Androgenetic alopecia	1 (2.22%)
14	Post herpetic neuralgia	2 (4.44%)
15	Post inflammatory hyperpigmentation	3 (6.67%)
16	Black hairy tongue	1 (2.22%)
17	Pigmented purpuric dermatoses	2 (4.44%)
18	Corn	1 (2.22%)

7. Vitamin D levels

7.1. Vitamin D status of the study population

Twenty eight (62.22%) cases and 20 (44.44%) controls had vitamin D deficiency (≤20ng/ml). The overall prevalence of vitamin D deficiency (≤ 20ng/ml) among the subjects was 53.33%. Though there was a 17.78% difference in the prevalence of vitamin D deficiency between the cases and control, it was not statistically significant (p=0.096). Only 8 (17.78%) subjects in each arm had normal vitamin D level (≥ 30 ng/ml). Nine (20%) cases and 17 (37.78%) controls had vitamin D insufficiency (20 to 30 ng/ml) (figure 16). Therefore the prevalence of vitamin D insufficiency / deficiency (≤ 30 ng/dl) in our study population was 82.22%.

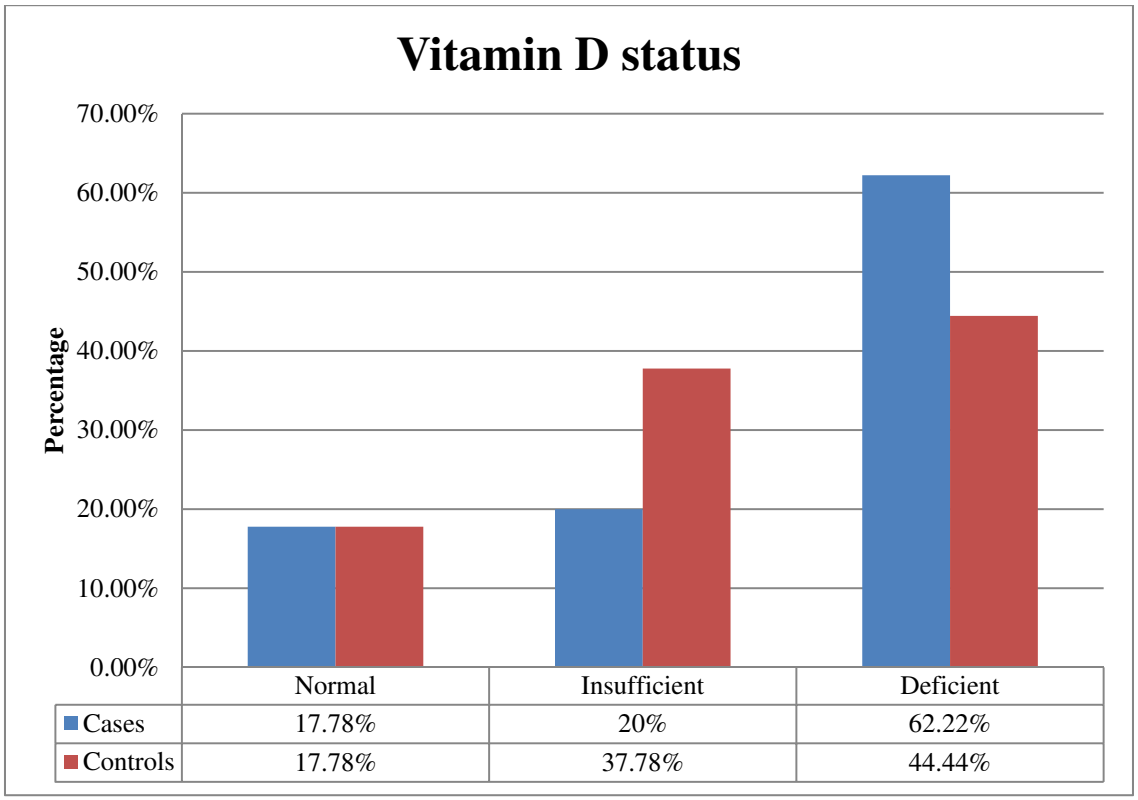


Figure 16: Vitamin D status of cases and controls

Table 11: Vitamin D status of the study population

Variable	Normal	Insufficient	Deficient
[Frequency (%)]			
Cases	8(17.78)	9 (20)	28 (62.22)
Controls	8(17.78)	17(37.78)	20 (44.44)
Odds ratio (95% confidence interval)	-----	2.06(0.82 – 5.21)	0.38 (0.14 – 1.08)
p - value	----	0.09	0.06

The mean vitamin D level (ng/ml) among the cases was 21.54 ± 9.41 and that of the controls was 21.24 ± 10.97 ($p = 0.64$). The cases and controls were further categorised into two groups (table 12) based on the presence (≤ 20 ng/ml) or absence of vitamin D deficiency (> 20 ng/ml).

Table 12: Vitamin D deficiency of the study population

Variable	Deficiency (≤ 20ng/ml)	No deficiency (> 20 ng/ml)
Cases [Frequency (%)]	28 (62.22)	17 (37.78)
Controls [Frequency (%)]	20 (44.44)	25 (55.56)

Odds ratio – 2.14; 95% Confidence interval - (0.87 – 5.26); p – value = 0.096

The psoriatic patients had a 2.14 times higher risk of vitamin D deficiency as compared to our controls. However this difference was not found to be statistically significant (odds ratio 2.14, 95% confidence interval 0.87 – 5.26, $p = 0.096$).

7.2 Correlation of vitamin D with baseline characteristics of the study subjects

7.2a Correlation of vitamin D with gender and age

Thirty one (60%) of the 52 men and 17 (45%) of the 38 women enrolled in this study were found to have vitamin D deficiency. There was no statistically significant difference between the prevalence of vitamin D deficiency among men and women (p = 0.1623). Table 13 shows the correlation of vitamin D deficiency with gender of the study subjects.

There was no significant correlation of vitamin D level with the age of the study subjects (r = 0.169, p = 0.11).

Table 13 - Correlation of vitamin D status with gender

Variable	Male [Frequency (%)]	Female [Frequency (%)]	p value
Vitamin D deficiency	31 (60)	17 (45)	0.1623
No vitamin D deficiency	21 (40)	21 (55)	

7.2b Correlation of vitamin D level with locality and skin type among the study subjects

The mean serum vitamin D level of the study subjects from semi-urban set up was 16.44± 1.63 ng/dl and that of those from rural set up was 23.57± 1.48 ng/ dl. This difference was statistically significant (p = 0.0004).

The mean serum vitamin D level of the subjects with type IV skin was 18.18 ± 8.88 ng/ml and that of subjects with type V skin was 22.30 ± 10.38 ng/ ml and the difference was not

statistically significant. Table 14 shows the correlation of vitamin D level with locality and skin type of the study subjects.

Table 14: Correlation of vitamin D level with locality and skin type

Variable	Mean vitamin D level (ng/dl)	*p* - value
Locality		0.0004
Semi-urban	16.44± 1.63	
Rural	23.57± 1.48	
Skin type		0.1162
Type IV	18.18 ± 8.88	
Type V	22.30 ± 10.38	

7.2c Correlation of vitamin D status with type of occupation and sun-exposure among the study subjects

Among the study subjects, there were 38 (42.22%) outdoor workers and 52 (57.78%) indoor workers. Fifteen (39.47%) of the outdoor workers and 33(63.5%) of the indoor workers were found to have vitamin D deficiency. A positive correlation of indoor occupation with vitamin D deficiency was noted and it was found to be statistically significant ($p = 0.024$).

Figure 17 shows the correlation of vitamin D status with the type of occupation.

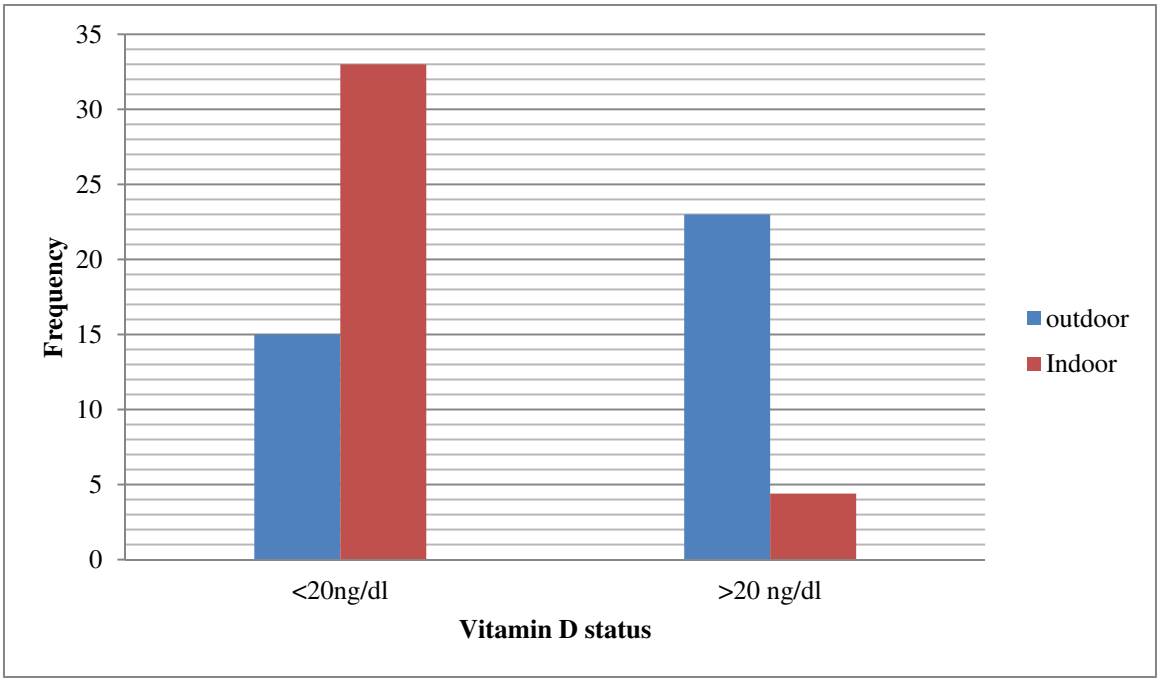


Figure 17: Correlation of vitamin D status with type of occupation

Thirty two (32.56%) of the 90 study subjects, reported average sun-exposure less than 30 minutes per day. Among them, 22(68.8%) were found to have vitamin D deficiency. Among the 58 subjects with average sun-exposure more than 30 minutes per day, vitamin D deficiency was noted in 26 (44.83) subjects (table 15). This difference was found to be statistically significant (p = 0.03).

Table 15 – Correlation of vitamin D level with occupation and sun-exposure

Variable[Frequency (%)]	Vitamin D ≤ 20ng/dl	Vitamin D >20ng/dl	p - value
Occupation			
Indoor	33(63.5)	19 (36.5)	**0.02**
Outdoor	15 (39.47)	23 (60.53)	
Sun-exposure			
Inadequate	22(68.75)	10 (31.25)	**0.03**
Adequate	26(44.83)	32(55.17)	

7.2d Correlation of vitamin D level with smoking among the study subjects

There was no statistical difference (p = 0.07) between the mean serum vitamin D level of smokers (16.08± 7.11 ng/ml) and non-smokers (21.98 ± 10.31 ng/ml).

Since there were only 9 subjects who consumed alcohol out of which 6 of them consumed alcohol only occasionally, it was not analysed.

7.3 Correlation of vitamin D level with type of clothing and sun-exposure among cases

The mean serum vitamin D level was only 14.48 ± 6 ng/ml among those who wore covered type of clothing whereas the corresponding level among those whose clothing allowed more of photo-exposure was 23.23 ± 10.28 ng/dl (p = 0.0001).

Among the 14 psoriatic patients who wore covered type of clothing, 12 (85.7%) of them had vitamin D deficiency. Among the 31 psoriatic patients whose clothing allowed more of photo-exposure, 16 (51.6%) of them had vitamin D deficiency and this difference was found to be statistically significant (p = 0.02). Figure 18 shows the correlation of the type of clothing with the vitamin D status of the cases.

The average duration of sun-exposure per day showed a positive correlation with the serum level of vitamin D and it was found to be significant (r = 0.5013, p = 0.0005).

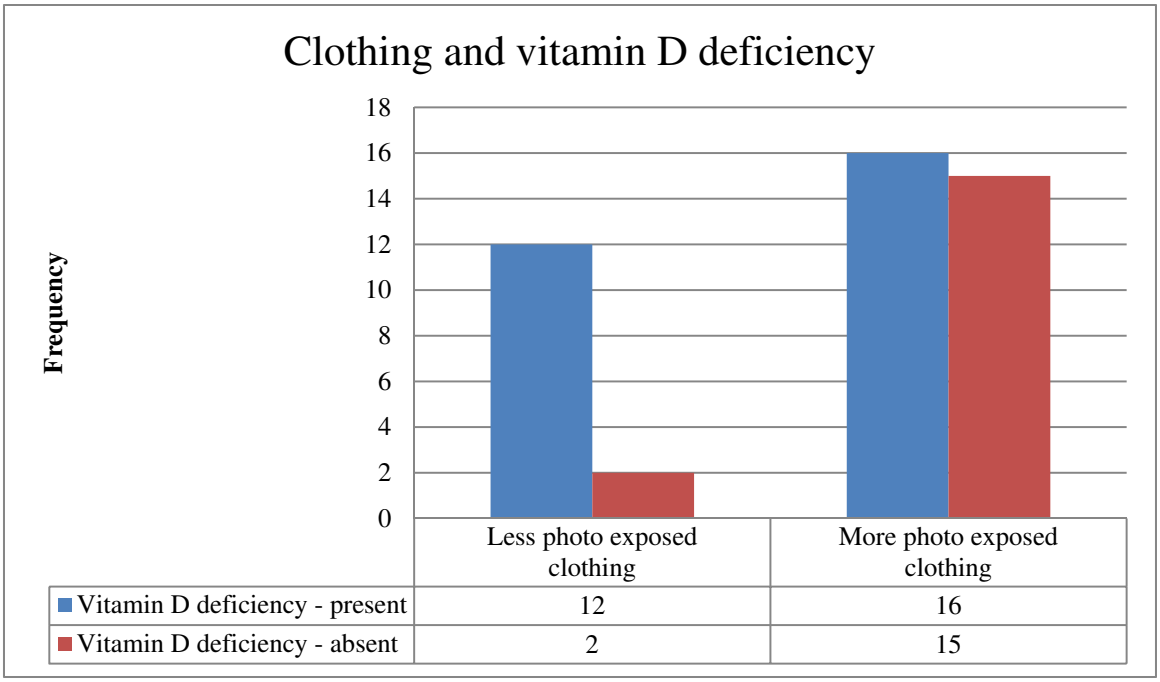


Figure 18: Clothing and vitamin D deficiency among cases

7.4. Correlation of type 1 and type 2 psoriasis with vitamin D level

The mean vitamin D level was lower among patients with type 1 psoriasis (19.56 ± 9.8ng/ml) as compared to those with type 2 psoriasis (25.86 ± 12.99). However the difference was not statistically significant ($p = 0.15$).

7.5. Correlation of vitamin D status with arthritis and nail involvement among the psoriatic patients

Of the 5 patients with arthritis, 2 of them had vitamin D deficiency. Since the number of patients with arthritis was low, it could not be analysed further. Nineteen of the 30 patients with nail involvement (63.33%) had vitamin D deficiency which was not statistically significant ($p = 0.50$).

7.6. Correlation of vitamin D level with disease duration, BSA involvement and PASI among patients

The disease duration showed a negative correlation with vitamin D level which showed tendency towards statistical significance (r = -0.2978, p = 0.047). So with an increase in disease duration there is a tendency towards decrease in vitamin D level.

The BSA involvement did not show significant correlation with vitamin D level (r = 0.2014, p = 0.18). Similarly PASI also did not show any significant correlation with vitamin D levels (r = 0.2598, p = 0.08). Table 16 shows the correlation of vitamin D level with sun-exposure, disease duration and disease severity.

Table 16: Correlation of vitamin D with sun-exposure, disease duration, BSA and PASI

Variable	Correlation with vitamin D level r	p – value
Average sun-exposure / day	0.5013	**0.0005**
Disease duration	-0.2978	0.047
BSA involvement	0.2014	0.18
PASI	0.2598	0.08

7.6. Correlation of vitamin D level with metabolic syndrome related parameters among the psoriatic patients

The BMI (r = -0.300, p = 0.045) and fasting blood sugar (r = -0.319, p = 0.037) showed a negative correlation with serum vitamin D level. With the increase in BMI and fasting blood

sugar, there was decrease in the serum vitamin D level. The HDL level of the cases showed a positive correlation with vitamin D level (r = 0.34, p =0.026).

The waist circumference (r = -0. 257, p = 0.09), systolic (r = -0.209, p = 0.17) and diastolic blood pressure (r = -0.134, p = 0.38) as well as triglyceride levels (r = -0.043, p = 0.78) did not show any significant correlation with the vitamin D level.

Table 17 shows the correlation of vitamin D level with BMI, central obesity, blood pressure, fasting blood sugar, HDL and triglycerides.

Table 17: Correlation of vitamin D level with metabolic syndrome related parameters

Variable	Correlation with vitamin D level r	p - value
Body mass index	-0.300	0.045
Fasting blood sugar	-0.319	**0.037**
Waist circumference	-0. 257	0.09
Systolic blood pressure	-0.209	0.17
Diastolic blood pressure	-0.134	0.38
HDL	0.340	**0.026**
Triglycerides	-0.043	0.78

The mean serum vitamin D level of the cases with metabolic syndrome was 24.53 ± 12.79 ng/ml whereas the mean serum level of the psoriatic patients without metabolic syndrome was 18.09 ± 7.96 ng/ ml. However this difference was not found to be significant ($p = 0.096$).

7.8. Multivariate analysis with logistic regression of vitamin D level with psoriasis, clothing, skin type, locality, occupation, sun-exposure and BMI

A logistic regression analysis of vitamin D level with psoriasis, clothing, skin type, locality, occupation, duration of sun-exposure per day and BMI was performed. The results are summarised in table 18. The presence of psoriasis was not associated with changes in vitamin D level after adjusting for clothing, skin type, locality, occupation, sun-exposure and BMI.

When compared to wearing more covered type of clothing, more photo-exposed type of clothing was shown to increase the serum vitamin D level by 47% after adjusting for skin type, locality, occupation, duration of sun-exposure and BMI.

When compared to residing in a semi-urban locality, residing in a rural locality was shown to increase the serum vitamin D level by 24% after adjusting for clothing, occupation, duration of sun-exposure and BMI.

Table 18 -Multivariate analysis with logistic regression of vitamin D level with psoriasis, clothing, skin type, sun-exposure, BMI, locality and occupation

Variable	Coefficient β	Standard error	*p* - value	95% confidence interval	β back transformed
Cases (vs. controls)	0.0368638	0.0979007	0.707	-0.1578919 to 0.2316195	4%
Clothing-Moderate photo-exposed (vs. minimal)	0.3886164	0.1200021	**0.002**	0.149894 to 0.6273388	**47%**
Skin type V(vs. type IV)	0.0078483	0.1166093	0.947	-0.2241249 to 0.2398214	0.8%
Duration of sun-exposure per day	0.0175861	0.0282195	0.535	-0.0385516 to 0.0737238	2%
BMI	-0.0085946	0.0092873	0.357	-0.0270699 to 0.0098808	0.9%
Rural (vs. semi-urban)	0.2174402	0.1009797	**0.034**	0.0165594 0.418321	**24%**
Indoor occupation (vs. outdoor)	-0.0778305	-0.0778305	0.565	-0.3455057 to 0.1898447	7%

Note - Skewed variables were log transformed and back-transformed, and interpreted as percentage change. R-squared = 28.16%

Discussion

Vitamin D is now recognised as a hormone that has pleiotropic actions on various cells and tissues in the body.(63) Recent research has implicated vitamin D deficiency with a number of chronic conditions, including autoimmune disorders such as multiple sclerosis, lupus erythematosus and dermopathies such as psoriasis.(86) The recent discovery of the role of vitamin D in modulating the immune system especially the Type 1 helper T cell (Th1) pathway shows its potential in treating Th1 related inflammatory diseases. Psoriasis is a Th1 immune mediated genetically determined common disorder affecting the skin, nails, joints and it has various systemic associations.(25) There are recent studies that show vitamin D deficiency in psoriasis patients more than in controls.(10–13)

Psoriasis is also a systemic disease centered on inflammation and involvement of cytokines of the Th1 pathway. Metabolic syndrome also involves a proinflammatory state and there is increased prevalence of metabolic syndrome in psoriasis. Fu and Vender have proposed the idea of the potential use of oral vitamin D to treat psoriasis and metabolic syndrome concurrently.(87)

There were no known published Indian studies on the relationship between vitamin D deficiency and psoriasis at the time of commencement of this study, which prompted us to undertake this prospective observational case-control study.

1. Demographic profile

In our study, the mean age of the cases was 41.62 years (± 37.92) and that of the control group was 41.29 years (± 37.56). This was almost the same as that reported by Gutte et al. from Mumbai.(17) When compared with the studies in western countries, the mean age was around 2 to 3 years lower than that reported in the studies from Spain(11,12) and Egypt(39) and 10 years lower than that reported from Italy.(13) The male : female ratio in our study was 1.4 : 1 which was consistent with the fact that there is male preponderance of the disease.(25)

There was no correlation of vitamin D level with age or gender among our study group. Orgaz-Molina et al., in their study found a negative correlation of vitamin D level with age of their patients ($r = -0.477$, $p = 0.001$).(11) Bentli et al., in their study reported female gender to be an independent predictor of vitamin D deficiency.(88) Johnson et al., in their study on the impact of gender on vitamin D status in morbidly obese individuals, noted a higher rate of vitamin D deficiency in men as compared to women (56% versus 47%; $p < 0.001$).(89) In our study higher proportion of men (60%) had vitamin D deficiency as compared to women (45%) which however did not reach a level of statistical significance ($p = 0.1623$).

Majority of our study subjects (57.78%) were from semi-urban areas. There was only one individual from an urban set up (1.11%) and 41.11% were from rural set up. The study from Spain by Orgaz- Molina et al was in a metropolitan set up (11) and the others studies on psoriasis and vitamin D had not specified the locality. Most of our study subjects (57.78%) were engaged in indoor occupation. With the rapid urbanization there are lesser number of people engaged in outdoor occupations like agriculture.(90) This results in less of sun-exposure which is essential for the cutaneous synthesis of vitamin D in the body.

Our study subjects either had Fitzpatrick skin type IV or V, with the type V skin being more common (77.78%). Melanin is an effective natural sunscreen. Because of the effective absorption of UVB photons by melanin, dark-skinned individuals require longer duration of exposure to sunlight to make the same amount of vitamin D_3, when compared with light-skinned individuals. It has been shown that a young adult with skin type III who was exposed to 1 minimal erythema dose (MED) of 54 mJ/cm^2 exhibit a 50-fold increase in serum vitamin D_3 within 8 hours. An adult of the same age with skin type V when exposed to 54 mJ /cm^2 did not show any significant rise in circulating concentrations of vitamin D_3. He required 5-10 times the exposure and exhibited only a 30-fold increase in the blood concentration of vitamin D_3.(91) The skin type was not documented in the study by Gutte et al.(17) Among the other reported studies, the study by Gisondi et al.(13) included white-skinned (Fitzpatrick type not specified). In a study by Orgaz -Molina et al.,(11) they included all the 6 skin types with fairly equal numbers with type (I to III) and (IV to V) and another study by the same authors (12) included those with skin types II to IV. The study by Hesham Abd El-Moaty Zaher et al.(39) from Egypt included skin types III to V. However the data on correlation of vitamin D level with the skin type were not available for comparison with the results in our study.

Table 19 shows comparison of demographic profile of study subjects as reported in studies on vitamin D deficiency and psoriasis.

Table 19 – Comparison of demographic profile of study subjects on vitamin D deficiency and psoriasis

Parameter	Our study	Orgaz-Molina et al.(11) Study 1	Orgaz Molina et. al (12) Study 2	Gisondi et al(13)	Hesham Abd El-Moaty Zaher et al(39)	Gutte et al.(17)
Country	India	Spain	Spain	Italy	Egypt	India (Mumbai)
Study period	December 2013- August 2014	July – August 2011	May – June 2011	December 2000 - December 2010	Published in November 2013	Published in June 2014
Study duration	9 months	1.5 months	1 month	1year	NA	NA
Study design	Case- control	Case- control	Case -control	Case- control	Case- control	Case- control
Subjects (Number in each arm)	CPP and minor dermatological ailments (45,45)	CPP (no arthritis) & minor dermatological (46,46)	CPP and minor dermatological ailments (43,43)	CPP & Rheumatoid arthritis and healthy controls (145,112,141)	CPP & healthy controls (48,40)	Psoriasis (type not specified) and healthy controls (50, 50)
Matching	Age & sex	Age & sex	Age & sex	Not done	Age, sex, phototype & socio economic status	Age & sex
Age-years (mean±SD) Cases controls	41.62±12.33 41.2 ± 12.40	45.57±9.96 45.89± 10.06	44.33± 8.71 43.95±11.3	51.9 ± 13.3 51.4 ± 7.0	43.88±15.157 42.28 ± 13.602	41 42
M:F	1.4:1	1.3:1	1.9:1	1.7:1	1.3:1	1.08:1
Locality categories	Urban, semi-urban & rural	NA	Metropolitan	NA	NA	NA
Fitzpatrick type	IV & V	I to VI	II, III, IV	White- skinned	III, IV, V	NA

NA – Data not available; SD – Standard Deviation; CPP – Chronic Plaque Psoriasis

2. Comparison of data on sun-exposure

The hours of sun-exposure per week among the cases ranged from 1 hour 35 minutes to 56 hours and among the controls it ranged from 1 hour 10 minutes to 56 hours($p = 0.61$). The average hour of sun-exposure per week among the cases was 15 hours and the same among the controls was 17 hours. This was much less as compared to the studies (>24 hours/week) reported from Spain,(11,12) despite India being a land of sunshine. The other Indian study did not have the data on sun-exposure.(17)

Gisondi et al.(13), in their study had categorised the subjects into those with an average sun-exposure per day less than 30 minutes and more than 30 minutes. Seventy seven per cent of their cases and 76% of their controls had an average sun-exposure per day less than 30 minutes. On comparing with that data, we had 40% cases having less than 30 minutes of average sun-exposure per day and 44% controls having less than 30 minutes of average sun-exposure per day. Their control group, despite 76% of them with less sun-exposure had a mean serum vitamin D level of 37.1 ± 27.6 ng/ml. The corresponding level in our control group was only 21.24 ± 10.97ng/ml. The Fitzpatrick skin type of the study population could possibly be one of the reasons for this observation.

There is a wide variation in the sun-exposure due to latitude, time of day, season, atmospheric components, sunscreen use, clothing and skin pigmentation.(63) It has been noted that there is greater variability in personal ultraviolet (UV) light exposure resulting from personal behaviour like avoidance of sun-exposure, clothing, sunscreen usage than from ambient UV light exposure.(92) The reported studies on vitamin D and psoriasis(11–13,39) have taken into account the latitude, the duration of sun-exposure, seasonal variations and to a certain extent skin

pigmentation. However the data on sunscreen usage and clothing among the study subjects was not available in these reports.

Studies show that a sunscreen having a sun protection factor (SPF) of 8 reduces the capacity of the skin to produce vitamin D by 95% if applied in the ideal way.(91) However there are studies showing that in most individuals the sunscreen usage is far from what is ideal, making it an unlikely factor to majorly contribute to the vitamin D status of individuals.(92) There were only four (4.44%) sunscreen users in our study group, all of whom belonged to the control arm. Out of that only one person (1%) used it regularly. Hence further analysis was not possible on this parameter.

Clothing is one of the major factor affecting the cutaneous absorption of vitamin D. Dense woven fabrics significantly reduce the transmission of UV radiation than the loose-knit ones. A study looking at the effect of white and black fabrics on UV exposure found that black wool decreased UVB irradiation by 98.6% whereas white cotton reduced it by 47.7%. However, after 40 minutes of simulated sunlight or whole body irradiation in volunteers with up to 6 MEDs of UV radiation both the fabrics suppressed vitamin D synthesis completely.(63)

In our study we had categorised the type of clothing based on the area of skin that was photo-exposed into minimal, moderate and maximal as explained in detail in the methodology. Since there were only 6 subjects in the 'maximal' category, they were clubbed with the 'moderate' group during analysis. Among the cases there were 31.11% patients under the minimal photo-exposed category and 68.89% patients under the moderate category. Among the controls, there were 11.11% subjects under the minimal photo-exposed category and 88.89% subjects under the moderate photo-exposed category. This difference was found to be statistically significant. Many

psoriasis patients reported of wearing more covered type of clothing to avoid social stigma when they had lesions in the exposed parts. Thirty one per cent of our cases avoided social activities due to the presence of the disease.

Table 20 - Comparison of data on sun-exposure in various studies on vitamin D and psoriasis

Parameter	Present study	Orgaz Molina et al (11) Study 1	Orgaz Molina et. al (12) Study 2	Gisondi et al(13)	Hesham Abd El-Moaty Zaher et al(39)	Gutte et al.(17)
Country	India	Spain	Spain	Italy	Egypt	India
Year	December 2013- August 2014	July – August 2011	May – June 2011	December 2000 - December 2010	Published in November 2013	Published in June 2014
Sun-exposure (Hours/ week)	Median (range)	Mean (SD)	Mean (SD)	NA	NA	NA
cases	7(1.35, 56)	25.98 ± 16.42	25.99 ± 18.78			
controls	7(1.10,56)	23.87 ± 17.14	28.22 ± 20.33			
Sun-exp < 30 min. / day [Freq (%)]					Infrequent sun-exposure	
cases	18(40%)	NA	NA	112(77.2)	11 (22.9)	NA
controls	20(44.4)			107(75.9)	7 (17.5)	

NA – Data not available; SD – Standard Deviation; Sun-exp – Sun-exposure; Freq - Frequency

The mean serum vitamin D level was only 14.48 ± 6 ng/ml among those who wore covered type of clothing whereas the corresponding level among those whose clothing allowed more of photo-exposure was 23.23 ± 10.28 ng/dl. (p = 0.0001). Since the other studies on vitamin D and psoriasis did not have this data, we could not compare our observation. Considering the small sample size, probably further larger studies are needed to establish the role of type of clothing in the vitamin D status of the patients with psoriasis.

3. Dietary intake of food rich in vitamin D

Vitamin D intake in diet is very low in India because of the very low consumption of vitamin D rich foods, low use of supplements and absence of fortification .(93) Therefore most of the Indian studies on vitamin D do not provide the data on oral vitamin day intake as it has been found to be negligible.(93) We collected the data on oral vitamin D intake in the form of dairy products and fish. Among cases it ranged from 0 IU to 302 IU with a median of 16 IU. Among controls, it ranged from 2 IU to 101 IU with a median of 18 IU. In the study, by Orgaz-Molina et al.,(11) the mean oral vitamin D intake among the cases was 188.72 ± 136.83 IU and that among the controls was 172.92 ± 102.18 IU.

The Food and Nutrition Board recommended dietary allowance (RDA) for infants below one year of age is 400 IU daily. Between 1 and 70 years of age, the RDA is 600 IU and for elderly over 70 years of age, it increases to 800 IU(72). However it has been shown that > 90% of vitamin D synthesis depends on ultraviolet exposure (cutaneous synthesis).

4. Psoriasis patient profile

The age at onset of psoriasis in our study group ranged from 5 years to 60 years. The duration of psoriasis at the time of recruitment into the study ranged from 3 months to 52 years.

And the mean duration of the disease was 10.38 years and the median was 6 years. In the study by Orgaz- Molina et al.,(11) the mean duration of disease was 18.58 ± 11.81 years, which was higher than in our study group.

A significant proportion of our patients (73.33%) had type 1 or early onset psoriasis, despite having excluded all psoriatic patients aged less than 18 years in the study. In our study, early onset psoriasis did not correlate with the positive family history of psoriasis. Indian studies report a lower familial incidence of the disease. Bedi et al (94) reported positive family history of psoriasis in 14% of their patients, while Kaur (95) et al reported family history in only 2% of their patients. Eleven per cent patients gave a positive family history of psoriasis in our study.

Among our patients, 46.67% had not observed any seasonal variation in the disease activity. Forty per cent had winter exacerbation and 13.33% had summer exacerbation. Bedi et al from India found that 72% of patients had significant seasonal variations, of which 30% felt worse in winter, 16% in monsoon and 4% in summer while the rest (28%) had persisting lesions all through the year, with erratic fluctuations not attributable to any particular season.(94)

Eleven per cent of our patients had psoriatic arthritis. In a recent Indian study on the prevalence and clinical patterns of psoriatic arthritis by Kumar et al., 8.7% of the patients with psoriasis had psoriatic arthritis, the commonest being symmetric polyarthritis, which is similar to our data.(96) In the study correlating vitamin D status and psoriasis by Orgaz- Molina et al., the prevalence of psoriatic arthritis was 7%. In the study by Gisondi et al., it was much higher (40.7%). In both the studies, there was no correlation between the presence of arthritis and vitamin D deficiency.(12,13)

Two third of our patients with psoriasis were noted to have psoriasis related nail changes, the commonest change being pits and the data was comparable with the other Indian studies.(25) The NAPSI score among our patients ranged from 0 to 37. Orgaz – Molina et al. reported nail involvement in only 14% of their cases. There was no correlation with vitamin D deficiency and nail involvement as in our study.(12)

5. Disease severity measures (PASI and BSA involvement)

The PASI score among our cases ranged from 0.9 to 15.6. Majority (78%) of the patients had a PASI score less than 7. The mean PASI score was 5.27 ± 3.61 which was almost similar to the PASI score reported in the study by Orgaz – Molina et al. where it was 4.28 ± 4.38.(11) The reason for the low PASI score could be because of excluding all the cases on systemic therapy and phototherapy as per the inclusion criteria.

The BSA involvement among our patients ranged from 2% to 50%. Sixteen per cent patients had BSA involvement more than 10%. The mean BSA involvement in our study was 8.51 ± 9.26 %, which was marginally above the BSA involvement reported by Orgaz- Molina et al. which was 5.10 ± 7.08%.(11) The disease severity measures were not documented in the other Indian study.(17)

6. Metabolic syndrome related parameters

Metabolic syndrome is a cluster of the most important risk factors for heart attack namely, abdominal obesity, high cholesterol, diabetes & pre-diabetes, and high blood pressure.(44) It has a prevalence of 20 to 25% of the adult population. It is also referred to as 'Syndrome X', 'Deadly Quartet' or the 'Insulin Resistance Syndrome'.

Metabolic syndrome shares some common immunological mechanisms with psoriasis.

- Adipocytokines secreted by the intra-abdominal fat cells affect glucose metabolism and promote inflammation. This causes elevated levels of interleukin-6 (IL-6), tumor necrosis factor alpha (TNF-α) and plasminogen activator inhibitor type1. These levels have been found to be elevated in psoriasis as well.
- Leptin, a hormone secreted by adipocytes plays a pro inflammatory role in regulating cytokine expression which modulates the Type 1 and Type 2 helper cells. Hyperleptinemia is found to be associated with the development of metabolic syndrome as well as with psoriasis.(45)
- Adiponectin, produced by adipocytes suppresses the production of TNF-α, IL-6 and INF-α. It has anti atherogenic effects and improves insulin sensitivity. Visceral obesity causes hypoadiponectinemia, which in turn increases the proinflammatory cytokines favoring the development of psoriasis as well as atherosclerosis.
- Osteopontin, an inflammatory glycoprotein which exerts a Th1 cytokine effect is thought to play a role in atherogenesis. Psoriasis is found to be a risk for elevated levels of osteopontin.(46)
- Hyperinsulinemia in metabolic syndrome can possibly promote susceptibility to or severity of psoriasis by facilitating chronic inflammation and angiogenesis.
- PSORS2-4, CDKAL1, and ApoE4 implicated in the shared genetic susceptibility to both metabolic syndrome and psoriasis.(15)

The overall prevalence of metabolic syndrome in our study population was 42%. The mean BMI of our cases was 27.12 ± 5.68 and it was significantly more than that of our controls which was 24.68 ± 4.82. (p = 0.03) These values were similar to the results of Gisondi et al., where the mean BMI of cases and controls was 26.6 ± 4.1 and 24.0 ± 3.7 respectively (p = 0.001).(13) In the study by Orgaz – Molina et al., there was a tendency towards significance, that is BMI of 29.68 ± 7.07 among cases and 27.17 ± 4.45 among controls (p = 0.05).(12) The metabolic syndrome related parameters were not available in the Indian study.(17)

Central obesity was observed in 69% of the cases and 42% of the controls (p = 0.02).In a recent south Indian study, 45 % cases and 39% controls had central obesity (p = 0.05).(97) The mean waist circumference among our cases was 91.33 ± 13.18 cm and that of the controls was 84.49 ± 11.59 cm (p = 0.01). In the study by Orgaz - Molina et al., there was no significant difference between the waist circumference of the cases (97.57 ± 10.74 cm) and controls (94.58 ± 11.75cm).(11)

In our study, the mean systolic blood pressure as well as the diastolic blood pressure among the cases was significantly higher than that in the controls. It was 132 ± 17/85 ± 12 mmHg among cases and 120 ± 13 /78± 8 mmHg among the controls. (Systolic BP - $p < 0.001$, Diastolic BP - p = 0.001). However in the studies by Orgaz- Molina et al.(11) and Gisondi et al.(13) there was no significant difference in the blood pressure between the cases and controls. Armstrong et al.(98) in a systematic review and meta-analysis of observational studies on the association between psoriasis and hypertension, noted an odds ratio of 1.58 (95% confidence interval 1.42-1.76) for hypertension among patients with psoriasis compared to controls.

In contrast to the observation by Orgaz – Molina et al., there was no statistical difference between the cases and controls with respect to fasting blood sugar values and triglycerides in our study. In concordance with their study, there was no significant difference in the HDL levels between their cases and controls. However the mean HDL level was higher than that observed in our study. Our cases and controls had a mean HDL level of 40.71 ± 9.13 mg/dl and 39.85 ± 10.07mg/ dl respectively whereas their cases and controls had a mean HDL level of 52.52 ± 14.38 mg/dl and 54.54 ± 13.36 mg/dl respectively.(11)

Fifty one percent of our cases and 33% of our controls had metabolic syndrome. However it was not statistically significant ($p = 0.08$). Orgaz – Molina et al. had 30% cases and 17% controls having metabolic syndrome ($p = 0.143$).(11) The higher prevalence of metabolic syndrome was in concordance with the study by Madanagopalane et al. in south India where 44% of the patients with psoriasis were noted to have metabolic syndrome.(45)

The link between psoriasis and metabolic syndrome has clinical implications as it relates to the safety and efficacy of commonly used systemic medications. For example, more aggressive liver monitoring guidelines are recommended for psoriatic patients with components of the metabolic syndrome like obesity and diabetes who are taking methotrexate.(99) Of note, patients with psoriasis also have an increased frequency of non-alcoholic fatty liver disease.(100) Increasing BMI is known to be associated with a reduction in psoriasis treatment efficacy, especially with the non-weight based biologic therapies.(101) Emerging data suggest that systemic treatment of psoriasis may be associated with an improvement in the metabolic risk biomarkers.(102) Therefore an early screening and intervention including life style modifications in patients with psoriasis would have an impact on the patients' overall health.

7. Vitamin D

Vitamin D3 is now known to act on the vitamin D receptor (VDR) to regulate keratinocyte growth and differentiation. It also influences the immune functions of dendritic cells and T lymphocytes, which are the key players in the pathogenesis of psoriasis. Hence it is suggested that low levels of vitamin D may have important implications in the pathogenesis of psoriasis.(19) Table 21 compares the prevalence of vitamin D deficiency in our study with the other studies on vitamin D and psoriasis.

Table 21 – Prevalence of vitamin D deficiency in studies on vitamin D and psoriasis

Parameter	Present study	Orgaz-Molina et al. (11) Study 1	Orgaz-Molina et. al (12) Study 2	Gisondi et al.(13)	Hesham Abd El-Moaty Zaher et al.(39)	Gutte et al.(17)
Country	India	Spain	Spain	Italy	Egypt	India
Overall prevalence of vitamin D deficiency	53.33%	10.98%	17.4%	41.46%	13.64%	80%

The overall prevalence of vitamin D deficiency (≤ 20ng/ml) in our study subjects was 53.33%. Gutte et al, from India reported a prevalence of 80% in their study.(17) The two studies reported from Spain by Orgaz – Molina et al. showed a much lesser prevalence among their subjects (10.98% and 17.4%).(11,12) Hesham Abd El-Moaty Zaher et al. from Egypt (39) also reported vitamin D deficiency in only 13.64% of their subjects. The Italian study by Gisondi et al had a slightly higher prevalence (41.46%).(13) In the Indian scenario, a very high prevalence of

70 to 100% in general population has been reported.(73) The prevalence of vitamin D deficiency in our study was comparable with the previously reported studies from Tamil Nadu. Table 22 lists a few studies from India on vitamin D deficiency.

Table 22 - Few studies from India on vitamin D deficiency

Author (reference)	Year	Place of study	Study group	Total number	Vitamin D Deficiency (<20ng/ml)
Zargar et al.(103)	2007	Kashmir	Adults	92	83%
Vupputuri et al.(104)	2006	Delhi	Urban adults	105	94.3%
Garg et al.(105)	2013	Delhi	Adults≥50y	1346	91.3%
Paul et al.(106)	2008	Tamil Nadu	Post-menopausal women	150	50%
Paul et al.(59)	2010	Tamil Nadu	HIV with/without ART & controls	105	49.5%
Harinarayan et al.(107)	2004	Tirupathi	Adults	316	69.3%
Baidya et al.(108)	2012	Kolkata	Doctors	40	92.5%
Multani et al.(109)	2010	Mumbai	Urban adults	214	87.5%
Marwaha et al.(110)	2011	Delhi	College girls	96	100%

(HIV – Human Immunodeficiency Virus infection; ART – Anti Retroviral Therapy)

In our study group, 62.22% cases and 44.44% controls were noted to have vitamin D deficiency (p value = 0.096). Though there was a 17.78% difference in the prevalence of vitamin D deficiency between the cases and control due to the overall high prevalence of vitamin D deficiency, our sample size was not sufficient to show any significant difference between the groups. In the studies by Gutte et al., Orgaz – Molina et al., Gisondi et al and Hesham Abd El-Moaty Zaher et al., there was statistically significant difference in the prevalence of vitamin D deficiency between the cases and controls as shown in the table 23.(11–13,17,39,40)

Our sample size was calculated based on the Italian study(13). In their study, only 30% of their controls had vitamin D deficiency whereas in our study, 44 % of our controls had vitamin D deficiency. This is probably a reflection of the overall high prevalence of vitamin D deficiency in Indian set up.

Wilson et al., however have reported 33% of psoriasis patients versus 34.9% non-psoriatic individuals having vitamin D deficiency (p value = 0.67). This was an US population based survey of 5841 individuals aged between 20 and 59 years, where the diagnosis was based on self-reported psoriasis.(41)

The mean serum vitamin D level (ng/ml) among our cases was 21.54 ± 9.41 and that of our controls was 21.24 ± 10.97 (p = 0.64). The mean serum vitamin D level among our patients was similar to that observed in the studies by Gisondi et al.(13) and Hesham Abd El-Moaty Zaher et al.(39) However in their studies, their controls had a mean serum level of approximately 37 ng/ml and in our study, it was only 21 ng /ml. Gutte et al. reported a mean serum level of 13.53 ±3.43 ng/ml among cases and 20.80 ± 14.37 ng/ml among the controls.(17) Nawaf et al. from Kuwait had reported much higher mean serum values among their study subjects

(31.5±14.41 ng/ml among cases and 53.5±19.6 ng/ml among controls).(40) Since in their study they had used different reference values for vitamin D deficiency as well for metabolic syndrome related parameters, their data could not be used for comparison.

Table 23 – Comparison of data on vitamin D deficiency in patients with psoriasis in various studies

Parameter	Present study	Orgaz-Molina et al.(11) Study 1	Orgaz - Molina et al. (12) Study 2	Gisondi et al(13)	Hesham Abd El-Moaty Zaher et al(39)	Gutte et al.(17)
Country	India	Spain	Spain	Italy	Egypt	India
VitD deficiency [Frequency(%)						
Case	28(62.22)	9 (19.6)	11(25.6)	81(57.8)	12(25)	48 (96)
Control	20 (44.44)	0(0)	4(9.3)	42(29.7)	0	32 (64)
p- value	0.096	.000	0.043	0.001	0.001	<0.001
Vit D (ng/ml) (mean±SD)						
Cases	21.54±9.41	30.52 ± 9.29	24.41 ± 7.80	20.7 ± 11.3	21.05±3.66	13.55±3.43
Controls	21.24± 10.97	38.31 ± 9.56	29.53 ± 9.38	37.1 ± 27.6	37.02±5.06	20.80±14.37
p- value	0.64	0.000	0.007	0.001	0.000	<0.001

SD – Standard Deviation; Vit D – vitamin D

Clothing pattern correlated significantly with the vitamin D level of our patients. The mean serum vitamin D level was only 14.48 ± 6 ng/ml among those who wore covered type of clothing whereas the corresponding level among those whose clothing allowed more photo-exposure was 23.23 ± 10.28 ng/dl ($p = 0.0001$).

However the above mentioned studies did not have these parameters documented for comparison. Zargar et al.(103), in a study on the vitamin D status of apparently healthy adults in Kashmir have noted that the surface area of skin exposed affects the vitamin D status.

The mean serum vitamin D level of our study subjects from semi-urban set up was 16.44± 1.63 ng/dl and that of those from rural set up was 23.57± 1.48 ng/ dl.(p = 0.0004). Harinarayan et al. in a south Indian study showed that the prevalence of vitamin D deficiency was more in subjects from urban set up (85.6%) as compared to rural set up (58.6%)(107). However Zargar et al., in their study from Kashmir did not find any significant difference among the rural (80%) and urban (85.7%) subjects.(103)

In concordance with the studies by Orgaz -Molina et al.(11) and Gisondi et al.,(13) there was no correlation of vitamin D level with the psoriasis disease duration or disease severity measures like PASI and BSA involvement.

In our study the vitamin D level of the patients did not show significant difference with regard to type 1 and type 2 psoriasis. The other studies on vitamin D and psoriasis did not have the vitamin D correlation with early and late onset psoriasis for comparison. Park et al. in their study on vitamin D receptor gene polymorphisms (30) have reported a significantly higher frequency of ApaI polymorphism in patients with psoriasis than in healthy controls. This tendency was more accentuated in early onset psoriasis.

Orgaz -Molina et al., in their study had observed significantly lower levels of vitamin D in patients with metabolic syndrome (24.1 ± 7.5 ng/ml) as compared to those without metabolic syndrome (32.8 ± 8.9 ng/ml, p = 0.007).(11) In our study, the mean serum vitamin D levels of the patients with and without metabolic syndrome were 18.09 ± 7.96 ng/ ml and 24.53 ± 12.79 ng/ ml respectively. However this difference did not reach a level of statistical significance. (p = 0.096).

Orgaz -Molina et al.(11,12) also observed a negative correlation between the BMI and vitamin D level (r = -0.30, p =0.005).The BMI of our cases showed a tendency towards negative correlation with the vitamin D level (r = -0.300, p = 0.045). In discordance with their study, the waist circumference, blood pressure and triglyceride levels did not show any correlation with the vitamin D level. Fasting blood sugar level of our cases showed a negative correlation with vitamin D level in concordance with their study (r = -0.319, p = 0.037). The HDL level of our cases showed a positive correlation with vitamin D level (r = 0.34, p =0.026) whereas Orgaz-Molina et al. did not observe any correlation between vitamin D level and HDL cholesterol.(12)

In our study, logistic regression analysis of vitamin D level could not show any significant changes in vitamin D level due to the presence of psoriasis after adjusting for clothing, skin type, locality, occupation, sun-exposure and BMI. This could be because of the following factors. Our sample size was small with respect to the high prevalence of vitamin D deficiency in the general population. The type of clothing after adjusting for the other confounders including sun-exposure per day showed a significant association with the vitamin D level in our study. In the context of psoriasis, this has important implications, as in our study we

observed that the cases wore more photo-protected type of clothing to avoid social embarrassment. The other studies on psoriasis and vitamin D level have not included this factor which could have partly affected the overall observed difference between the cases and controls.

Our sample size was small and hence we could not arrive at a definitive conclusion regarding the difference in prevalence of vitamin D deficiency between the cases and controls, given the high prevalence of vitamin D deficiency in India.

As in other studies, our study showed a high prevalence of vitamin D deficiency among patients with psoriasis. However though most studies found the prevalence to be significantly higher in psoriasis patients than in controls, our study did not show a significant difference when compared with ethnically comparable controls. Further studies with larger sample size are needed to study the effect of vitamin D on the disease and whether psoriasis is an independent risk factor for vitamin D deficiency. In addition to studying the role of metabolic syndrome on the vitamin D status of patients with psoriasis, future studies could also include parameters such as social avoidance and the actual sun-exposure, due to clothing styles used by the patients with psoriasis.

Conclusions

In this hospital based prospective age and sex matched case - control observational study from Tamil Nadu on the vitamin D status of the patients with chronic plaque psoriasis in comparison with the controls with minor dermatological problems between December 2013 and August 2014, we observed the following.

- The overall prevalence of vitamin D deficiency (≤ 20ng/ml) in the study subjects was 53.33%.
- Sixty two per cent cases and 44% controls had vitamin D deficiency with the observed difference not being statistically significant (p value = 0.096).
- The mean serum vitamin D level was similar among the cases and controls, 21.54 ± 9.41ng/ml and 21.24 ± 10.97 respectively (p = 0.64).
- There was no correlation between vitamin D level and psoriasis disease severity measures like PASI and BSA involvement.
- There was no correlation between vitamin D level and duration of disease, presence of arthritis as well as nail changes.
- Logistic regression analysis did not show any significant changes in vitamin D level attributable to the presence of psoriasis after adjusting for clothing, skin type, locality, occupation, sun-exposure and BMI.

The other significant observations include:

- Patients with psoriasis were observed to wear a more covered type of clothing which could have an impact on their vitamin D level.

- More photo-exposed type of clothing was shown to increase the serum vitamin D level by 47% after adjusting for skin type, locality, occupation, duration of sun-exposure and BMI in a logistic regression analysis when compared to wearing more covered type of clothing
- Body mass index of the patients showed a tendency towards negative correlation with vitamin D level (r = -0.300, $p = 0.045$)
- HDL level of the cases showed a positive correlation with vitamin D level (r = 0.34, $p = 0.026$)
- Fasting blood sugar level of the cases showed a negative correlation with vitamin D level (r = -0.319, $p = 0.037$)
- Significantly higher mean serum level of vitamin D ($p = 0.0004$) was observed in patients from rural set up (23.57± 1.48 ng/ dl) as compared to those from semi-urban set up (16.44 ± 1.63 ng/dl).
- Residing in a rural locality was shown to increase the serum vitamin D level by 24% after adjusting for clothing, occupation, duration of sun-exposure and BMI when compared to residing in a semi-urban locality.
- Significantly higher proportion of indoor workers ($p = 0.02$) and those with average sun-exposure less than 30 minutes ($p = 0.03$) had vitamin D deficiency
- Dietary intake of vitamin D among most subjects was less than one tenth of the recommended dietary allowance.
- Significantly higher proportion of the cases had central obesity ($p = 0.02$) and hypertension ($p = 0.002$) as compared to controls.

Limitations

- Our sample size was small and hence we could not arrive at a definitive conclusion regarding the difference in prevalence of vitamin D deficiency between the cases and controls, given the high prevalence of vitamin D deficiency in India. Due to constraint of resources (time and finances), a larger sample size was not feasible.
- Since psoriatic patients on systemic therapy were not included in the study, patients with more severe disease could not be part of the study.
- Cases and controls were not recruited around the same season of the year due to practical difficulties. However, in southern India where this study was conducted, sunlight is abundant almost throughout the year.
- Serum Calcium, Parathyroid hormone (PTH) levels, Bone Mineral Density scan and C-reactive protein levels could not be done due to financial constraints.

Recommendations

- In view of the overall high prevalence of vitamin D deficiency in India, larger studies are needed to assess the difference in prevalence of vitamin D deficiency among patients with psoriasis and controls.
- The studies on vitamin D level should include the clothing pattern of the subjects.
- Fortification of food items with vitamin D is needed in the country given the prevalence of vitamin D deficiency in epidemic level.

Summary

Background

Psoriasis, now recognised as a systemic disease is centered on inflammation and involvement of cytokines of the Th1 pathway. There are recent studies showing higher prevalence of vitamin D deficiency in patients with psoriasis than in control groups.(10–13) Vitamin D acts on the vitamin D receptor (VDR) to regulate keratinocyte growth and differentiation. The discovery of the systemic role of vitamin D in the modulation of the immune system especially the Type 1 helper T cell (Th1) pathway suggests that low levels of vitamin D may have important implications in the pathogenesis of psoriasis.(19)

Objectives

Our primary objective was to determine the 25-hydroxyvitamin D status of patients with chronic plaque psoriasis in comparison with age and sex matched controls with non-psoriatic, non-photosensitive skin diseases presenting to the outpatient department (OPD) as a pilot study. Our secondary objective was to correlate the psoriasis disease characteristics with vitamin D level.

Methods

Forty-five consecutive consenting patients with chronic plaque psoriasis and 45 age and sex matched controls with minor dermatological diseases from Tamil Nadu were recruited in this study. Data on demographic profile, sun-exposure, sunscreen usage, smoking, alcohol, type of clothing, waist circumference, vitamin D level, fasting and post prandial sugars, total cholesterol, triglycerides, LDL and HDL were collected from all study participants. From the patients with

psoriasis, data on duration of disease, disease severity as assessed by BSA and PASI, presence of arthritis / nail changes were also collected.

Results

The overall prevalence of vitamin D deficiency (≤ 20ng/ml) in the study subjects was 53.33%. Sixty two per cent cases and 44% controls had vitamin D deficiency with the observed difference not being statistically significant (p value = 0.096). The mean serum vitamin D level was similar among the cases and controls, 21.54 ± 9.41ng/ml and 21.24 ± 10.97 respectively (p = 0.64). There was no statistically significant difference (p = 0.15) in the mean vitamin D level between patients with type 1 psoriasis (19.56 ±9.8 ng/ml) and type 2 psoriasis (25.86 ± 12.99 ng/ml). The mean serum vitamin D level was significantly (p = 0.0001) lower in patients who wore covered type of clothing (14.48 ± 6 ng/ml) when compared to the patients who wore clothing that allowed more photo-exposure (23.23 ± 10.28 ng/dl). With an increase in disease duration, there was a tendency towards decrease in vitamin D level (r = -0.2978, p = 0.047). There was no correlation between vitamin D level and psoriasis disease severity measures like PASI and BSA involvement. The vitamin D status of the patients did not differ between those with and without arthritis as well as between those with and without nail changes. The BMI (r = -0.300, p = 0.045) and fasting blood sugar (r = -0.319, p = 0.037) showed a negative correlation and the HDL level (r = 0.34, p = 0.026) showed a positive correlation with vitamin D level whereas waist circumference, systolic and diastolic blood pressure, triglyceride levels as well as metabolic syndrome did not show any significant correlation with the vitamin D level among cases.

Logistic regression analysis did not show any significant changes in vitamin D level attributable to the presence of psoriasis after adjusting for clothing, skin type, locality,

occupation, sun-exposure and BMI. In addition, the pattern of clothing was observed to be strongly associated with changes in vitamin D level after adjusting for confounders.

Limitation

Our sample size was small given the high prevalence of vitamin D deficiency in India and hence could not establish a significant difference in the prevalence of vitamin D deficiency between the cases and controls.

Conclusions

Higher proportions of patients with psoriasis were found to have vitamin D deficiency as compared to the controls, but not reaching a level of statistical significance. Clothing pattern may have a role in the observed difference in vitamin D status. Further studies with larger sample size are needed to assess the association between vitamin D status and psoriasis.

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Annexure

Annexure 1 – Informed consent for cases and controls - English

PATIENT INFORMATION SHEET

Vitamin D and Psoriasis Vulgaris

You are being requested to participate in a study on vitamin D and psoriasis. Psoriasis vulgaris is a long-term (chronic) skin problem that causes skin cells to grow too quickly, resulting in thick, white, silvery, or red patches of skin.

Recently a few studies done abroad have shown that patients with psoriasis have more chances of vitamin D deficiency than those without the disease. We would like to find out if similar problem exists in patients with psoriasis in India.

In this study, blood tests will be done to determine the vitamin D level, blood sugar level and cholesterol level. You will be requested to come in empty stomach for the blood tests. Five to 10ml blood will be collected from you, once in empty stomach and once 2 hours after breakfast. You may experience pain and minimal bleeding at the site where blood is drawn.

Your participation in this study is entirely voluntary and you can also decide to withdraw from this study. If you do so, this will not affect your usual treatment at this hospital in any way.

For all the participants in this study, the vitamin D test will be done free of cost.

Only those involved in the study will have access to your medical details. The results of this study may get published in a medical journal but your identity will not be revealed in any publication or presentation of results.

If you have any further questions, please ask Dr. Priya Jeevamani C (tel: 0416 228 2054) or email: derm@cmcvellore.ac.in

INFORMATION SHEET FOR CONTROL GROUP

Vitamin D and Psoriasis Vulgaris

You are being requested to participate in a study on vitamin D and psoriasis. Psoriasis vulgaris is a long-term (chronic) skin problem that causes skin cells to grow too quickly, resulting in thick, white, silvery, or red patches of skin.

Recently a few studies done abroad have shown that patients with psoriasis have more chances of vitamin D deficiency than those without the disease. We would like to find out if similar problem exists in patients with psoriasis in India. Though you do not have psoriasis, your participation in the study will help us to know the vitamin D status in patients without psoriasis for comparison.

In this study, blood tests will be done to determine the vitamin D level, blood sugar level and cholesterol level. You will be requested to come in empty stomach for the blood tests. Five to 10ml blood will be collected from you, once in empty stomach and once 2 hours after breakfast. You may experience pain and minimal bleeding at the site where blood is drawn.

Your participation in this study is entirely voluntary and you can also decide to withdraw from this study. If you do so, this will not affect your usual treatment at this hospital in any way.

For all the participants in this study, the vitamin D test, blood sugar level and cholesterol level will be done free of cost.

Only those involved in the study will have access to your medical details. The results of this study may get published in a medical journal but your identity will not be revealed in any publication or presentation of results.

If you have any further questions, please ask Dr. Priya Jeevamani C (tel: 0416 228 2054) or email: derm@cmcvellore.ac.in

Informed Consent form to participate in a research study

Study Title: Vitamin D and Psoriasis

Study Number: _____

Subject's Initials: _____ Subject's Name: _____

Date of Birth / Age: _____

(Subject)

(i) I confirm that I have read and understood the information sheet dated _____ for the above study and have had the opportunity to ask questions.

(ii) I understand that my participation in the study is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.

(iii) I understand that the Sponsor of the clinical trial, others working on the Sponsor's behalf, the Ethics Committee and the regulatory authorities will not need my permission to look at my health records both in respect of the current study and any further research that may be conducted in relation to it, even if I withdraw from the trial. I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published.

(iv) I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose(s).

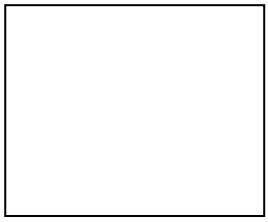
(v) I agree to take part in the above study.

Signature (or Thumb impression) of the Subject/Legally Acceptable

Date: _____/_____/_____

Signatory's Name: _____ Signature:

Or



Representative: _____

Date: _____/_____/_____

Signatory's Name: _____

Signature of the Investigator: _____

Date: _____/_____/_____

Study Investigator's Name: _____

Signature of the Witness: _____

Date: _____/_____/_____

Name & Address of the Witness: _____

Annexure 2 - Informed consent for cases and controls - Tamil

நோயாளிகளின் தகவல் தாள்

வைட்டமின் 'டி' மற்றும் ஸோரியாஸிஸ் பற்றியதான ஆய்வு

வைட்டமின் 'டி' மற்றும் ஸோரியாஸிஸ் பற்றியதான ஆய்வில் பங்கேற்க தங்களை வேண்டுகிறோம். ஸோரியாஸிஸ் என்பது தோல் அணுக்கள் விரைவாக வளர்வதன் காரணமாக ஏற்படும் செதில்களுடன் கூடிய நீண்ட கால தோல் நோய்.

சமீபத்தில் வெளி நாடுகளில் செய்யப்பட்ட ஒரு சில ஆய்வுகளில் ஸோரியாஸிஸ் நோயாளிகளுக்கு அந்த நோய் இல்லாதவர்களை விட வைட்டமின் 'டி' குறைபாடு ஏற்படும் வாய்ப்பு அதிகம் உள்ளது என்று கண்டறியப்பட்டுள்ளது. இந்தியாவில் உள்ள ஸோரியாஸிஸ் நோயாளிகளிடம் அவ்வித குறைபாடு உள்ளதா என்று கண்டறிய உள்ளோம்.

இந்த ஆய்வில், வைட்டமின் 'டி' அளவு, சர்க்கரை அளவு மற்றும் கொழுப்பு அளவு தீர்மானிக்க இரத்த பரிசோதனை செய்யப்படும். இதற்காக தாங்கள் வெறும் வயிற்றில் வருவது அவசியம். ஐந்து முதல் பத்து மி.லி. இரத்தம் தங்களிடமிருந்து உணவுக்கு முன் மற்றும் காலை உணவுக்கு இரண்டு மணி நேரத்திற்குப் பின் எடுக்கப்படும். இரத்தம் எடுக்கப்பட்ட இடத்தில் சிறிதளவு வலி மற்றும் இரத்தக் கசிவு வாய்ப்பு உள்ளது.

தாங்கள் இந்த ஆய்வில் பங்கேற்பது தங்களுடைய சுய விருப்பத்திற்கு உட்பட்டது. தாங்கள் இந்த ஆய்வில் இருந்து விலகவும் முடிவு செய்யலாம். இது இந்த மருத்துவமனையில் தாங்கள் பெறும் வழக்கமான சிகிச்சையை எந்த விதத்திலும் பாதிக்காது.

இந்த ஆய்வில் பங்கேற்கும் அனைவருக்கும் வைட்டமின் 'டி' சோதனை இலவசமாக செய்யப்படும்.

இந்த ஆய்வில் ஈடுபட்டு உள்ளோர் மாத்திரமே தங்கள் மருத்துவ விவரங்களை அறிய முடியும். இந்த ஆய்வின் முடிவுகள் ஒரு வேளை மருத்துவ பத்திரிக்கைகளில் வெளியிடப்பட்டாலும் தங்களுடைய அடையாளம் எந்த விதத்திலும் வெளியிடப்படாது.

இந்த ஆய்வைப் பற்றி மேலும் தகவல் பெற Dr. பிரியா ஜீவமணி அவர்களை அணுகலாம் - தொலைபேசி 0416 - 2282054; email: derm@cmcvellore.ac.in.

தகவல் தாள்

வைட்டமின் 'டி' மற்றும் ஸோரியாஸிஸ் பற்றியதான ஆய்வு

வைட்டமின் 'டி' மற்றும் ஸோரியாஸிஸ் பற்றியதான ஆய்வில் பங்கேற்க தங்களை வேண்டுகிறோம். ஸோரியாஸிஸ் என்பது தோல் அணுக்கள் விரைவாக வளர்வதன் காரணமாக ஏற்படும் செதில்களுடன் கூடிய நீண்ட கால தோல் நோய்.

சமீபத்தில் வெளி நாடுகளில் செய்யப்பட்ட ஒரு சில ஆய்வுகளில் ஸோரியாஸிஸ் நோயாளிகளுக்கு அந்த நோய் இல்லாதவர்களை விட வைட்டமின் 'டி' குறைபாடு ஏற்படும் வாய்ப்பு அதிகம் உள்ளது என்று கண்டறியப்பட்டுள்ளது. இந்தியாவில் உள்ள ஸோரியாஸிஸ் நோயாளிகளிடம் அவ்வித குறைபாடு உள்ளதா என்று கண்டறிய உள்ளோம். தங்களுக்கு ஸோரியாஸிஸ் நோய் இல்லாதிருப்பினும், தங்களை பரிசோதிப்பதன் மூலம் ஸோரியாஸிஸ் நோய் இல்லாதவர்களின் வைட்டமின் 'டி' நிலையை அறிய இயலும்.

இந்த ஆய்வில், வைட்டமின் 'டி' அளவு, சர்க்கரை அளவு மற்றும் கொழுப்பு அளவு தீர்மானிக்க இரத்த பரிசோதனை செய்யப்படும். இதற்காக தாங்கள் வெறும் வயிற்றில் வருவது அவசியம். ஐந்து முதல் பத்து மி.லி. இரத்தம் தங்களிடமிருந்து உணவுக்கு முன் மற்றும் காலை உணவுக்கு இரண்டு மணி நேரத்திற்குப் பின் எடுக்கப்படும். இரத்தம் எடுக்கப்பட்ட இடத்தில் சிறிதளவு வலி மற்றும் இரத்தக் கசிவு வாய்ப்பு உள்ளது.

தாங்கள் இந்த ஆய்வில் பங்கேற்பது தங்களுடைய சுய விருப்பத்திற்கு உட்பட்டது. தாங்கள் இந்த ஆய்வில் இருந்து விலகவும் முடிவு செய்யலாம். இது இந்த மருத்துவமனையில் தாங்கள் பெறும் வழக்கமான சிகிச்சையை எந்த விதத்திலும் பாதிக்காது.

இந்த ஆய்வில் பங்கேற்கும் அனைவருக்கும் வைட்டமின் 'டி', சர்க்கரை அளவு மற்றும் கொழுப்பு அளவு சோதனை இலவசமாக செய்யப்படும்.

இந்த ஆய்வில் ஈடுபட்டு உள்ளோர் மாத்திரமே தங்கள் மருத்துவ விவரங்களை அறிய முடியும். இந்த ஆய்வின் முடிவுகள் ஒரு வேளை மருத்துவ பத்திரிக்கைகளில் வெளியிடப்பட்டாலும் தங்களுடைய அடையாளம் எந்த விதத்திலும் வெளியிடப்படாது.

இந்த ஆய்வைப் பற்றி மேலும் தகவல் பெற Dr. பிரியா ஜீவமணி அவர்களை அணுகலாம் - தொலைபேசி 0416 - 2282054; email: derm@cmcvellore.ac.in.

ஒப்புதல் படிவம்

மருத்துவ ஆய்வில் பங்கேற்பதற்கான ஒப்புதல் படிவம்

தலைப்பு- ஸோரியாஸிஸ் மற்றும் வைட்டமின் டி பற்றிய ஆய்வு

ஆய்வு எண்:

பங்கேற்பவரின் பெயர்:

பிறந்த தேதி/வயது:

1. நான்..... தேதியில் மேற்கண்ட தகவல் படிவத்திலுள்ள அனைத்து தகவல்களையும் நன்கு படித்து அறிந்து கொண்டேன். இவ்வாராய்ச்சியின் நோக்கத்தையும் இதில் பங்கெடுத்துக்கொள்வதன் மூலம் ஏற்படும் நன்மைகளையும் அறிந்துகொண்டேன்.
2. இவ்வாராய்ச்சியில் பங்கு கொள்வது என் விருப்பம் சார்ந்தது என்பதனையும், இவ்வாராய்ச்சியில் இருந்து எப்போது வேண்டுமானாலும் எக்காரணமும் இன்றி விலகிக் கொள்ளலாம் என்பதனையும் அறிந்து கொண்டேன். என்னுடைய விலகல் என் மருத்துவ சிகிச்சைக்கான எந்தவொரு உரிமையையும் பாதிக்காது என்பதையும் அறிவேன்.
3. இவ்வாராய்ச்சி சம்பந்தமான பொறுப்பில் உள்ளவர்கள், சட்டப்பூர்வமான குழுவை சார்ந்தவர்கள் மற்றும் ஒழுங்குமுறை குழுவை சார்ந்தவர்கள் மற்றும்மருத்துவஒழுங்குமுறை குழுவை சார்ந்தவர்கள், என்மருத்துவ பதிவேடுகளை என்னுடைய அனுமதியின்றி கையாளலாம் என்பதற்கு எனது அனுமதியை தெரிவித்துக்கொள்கிறேன். இதில் எனக்கு எந்த மறுப்பும் இல்லை.
4. இவ்வாராய்ச்சியின் தகவல்கள் மற்றும் முடிவுகள் அறிவியல் சம்பந்தமாக பயன்படுத்துவதில் எனக்கு எந்த மறுப்பும் இல்லை.
5. நான் இவ்வாராய்ச்சியில் பங்கு கொள்ள முழுமனதுடன் சம்மதிக்கிறேன்.

நோயாளி/ சட்டபூர்வ அனுமதி அளிக்கப்பட்டவரின் கையொப்பம்/கைரேகை

பங்கேற்பவரின் பெயர்..... தேதி.....

பரிசோதிப்பவர் பெயர்.....

சாட்சியாளரின் கையொப்பம்/ பெயர்.....தேதி.....

Annexure 3 – Clinical research form for cases

CLINICAL RESEARCH FORM

Vitamin D deficiency and Psoriasis Vulgaris

Study ID ☐☐☐ Hospital Num. ☐☐☐☐☐☐☐ Date _ _ / _ _ / 201 _

Age ☐☐ Sex (1-M, 2-F) ☐ Locality (1-Urban, 2-Semi-Urban, 3-Rural) ☐

Occupation (1-Outdoor, 2-Indoor) ☐ Fitzpatrick Skin Type (3, 4, 5, 6) ☐

Avg. Sun hours: week day (hh:mm) ☐☐:☐☐ week end (hh:mm) ☐☐:☐☐

Sun screen usage (1-Always, 2-Mostly, 3-Occasional, 4-Never) ☐ SPF (if used) ☐☐

Clothing (1 Face, 2 Hand/Feet/Neck, 3 Forearms, 4 Waist, 5 Legs) ☐

Family history of Psoriasis (1-Yes, 0-No, 2-Doubtful) ☐

Smoking (1-Yes, 0-No) ☐ If yes, avg. Cigars/day ☐☐.☐☐ No. of years ☐☐

Alcohol (1-Yes, 0-No) ☐ If yes, frequency (1-Daily, 2-Weekly, 3-Monthly, 4-Occational ☐

Avg. quantity alcohol/week (in ml.) ☐☐☐☐ No. of years of alcohol ☐☐

Avg./week: Fish (gms) ☐☐☐☐ Milk (ml) ☐☐☐☐ Milk fortified (1-Yes,0-No) ☐

Diabetic (1-Y,0-N) ☐ If yes, num yrs ☐☐.☐☐ Treatment (1-Drugs, 2-Diet) ☐

Hypertensive (1-Yes, 0-No) ☐ If yes, duration (in years) ☐☐.☐☐

Dyslipidemia (1-Yes, 0-No) ☐ If yes, treatment (1-Drugs, 2-Diet control) ☐

Weight (kg) ☐☐☐.☐☐ Height (cms) ☐☐☐ BMI ☐☐.☐☐

BP1 ☐☐☐/☐☐☐ BP2 ☐☐☐/☐☐☐ AC ☐☐☐ PC ☐☐☐

Waist (cms) ☐☐☐.☐ Total Cholesterol ☐☐☐ Triglycerides ☐☐☐

HDL ☐☐ LDL ☐☐☐ Vitamin D level ☐☐.☐☐

Is Control? (1-Yes, 0-No) ☐

Onset age ☐☐ Exacerbation (0-No Season, 1-Winter, 2-Summer) ☐

Avoidance due to ds? (1-Y, 0-N) ☐ Reason (1-Social, 2-Disability, 3-Others) ☐

Topical treatment ☐☐ ----------

Systemic treatment ☐☐ ----------

Phototherapy in last one year (1-Yes, 0-No) ☐

Nail Involvement (1-Yes, 0-No) ☐ NAPSI score ☐☐☐

Arthritis (1-Yes, 0-No) ☐ Caspar Score ☐ Moll & Wright type ☐

Is Arthritis Symptomatic now? (1-Yes, 0-No) ☐

Total BSA involvement in percentage ☐☐.☐☐

PASI ☐☐.☐☐

The Psoriasis Area and Severity Index (PASI) is a quantitative rating score for measuring the severity of psoriatic lesions based on area coverage and plaque appearance.

Plaque characteristic	Lesion score	Head	Upper Limbs	Trunk	Lower Limbs
Erythema	0 = None 1 = Slight 2 = Moderate 3 = Severe 4 = Very severe				
Induration/Thickness					
Scaling					
Add together each of the 3 scores for each body region to give 4 separate sums (A).					
Lesion Score Sum (A)					

Percentage area affected	Area score	Head	Upper Limbs	Trunk	Lower Limbs
Area Score (B) *Degree of involvement as a percentage for each body region affected (score each region with score between 0-6)*	0 = 0% 1 = 1% - 9% 2 = 10% - 29% 3 = 30% - 49% 4 = 50% - 69% 5 = 70% - 89% 6 = 90% - 100%				
Multiply Lesion Score Sum (A) by Area Score (B), for each body region, to give 4 individual subtotals (C).					
Subtotals (C)					
Multiply each of the Subtotals (C) by amount of body surface area represented by that region, i.e. x 0.1 for head, x 0.2 for upper body, x 0.3 for trunk, and x 0.4 for lower limbs.					
Body Surface Area		**x 0.1**	**x 0.2**	**x 0.3**	**x 0.4**
Totals (D)					
Add together each of the scores for each body region to give the final PASI Score.					

PASI Score = ☐

NAPSI* Score

Instructions for grading psoriatic nails using NAPSI

Nail Matrix Evaluation
In each quadrant of the nail, nail matrix psoriasis is evaluated by presence of *any* of the nail matrix features (pitting, leukonychia red spots in the lunula, crumbling).

Nail Bed Evaluation
Nail bed psoriasis is evaluated by the presence of *any* of the nail bed features (onycholysis, splinter haemorrhages, subungual hyperkeratosis, oil drop (salmon patch dyschroma).

1. The nail is divided with imaginary horizontal and longitudinal lines into quadrants. Each nail is given a score for nail bed psoriasis (0-4) and nail matrix psoriasis (0-4) depending on the presence of any of the features of nail psoriasis in that quadrant.
2. Each nail gets a matrix score and a nail bed score, the total of which is the score for that nail (0-8).
3. Each nail is evaluated, and the sum of all the nails is the total NAPSI score. The sum of the scores from all nails is 0-80; or 0-160 if toenails are included.

Score for **matrix** psoriasis: 0 = none, 1 = present in 1/4 nail, 2 = present in 2/4 nail, 3 = present in 3/4 nail, 4 = present in 4/4 nail
Score for **nail bed** psoriasis: 0 = none, 1 = present in 1/4 nail, 2 = present in 2/4 nail, 3 = present in 3/4 nail, 4 = present in 4/4 nail

Matrix Psoriasis

Score: _____ _____ _____ _____ _____

Matrix Psoriasis

Score: _____ _____ _____ _____ _____

Nail Bed Psoriasis

Score: _____ _____ _____ _____ _____

Nail Bed Psoriasis

Score: _____ _____ _____ _____ _____

Total Score per nail

Sum: _____ _____ _____ _____ _____

Total Score per nail

Sum: _____ _____ _____ _____ _____

* NAPSI: Nail Psoriasis Severity Index

Total NAPSI Score

Arthritis

Moll and Wright subgroups

1	DIP joint only
2	Asymmetrical oligoarthritis
3	Polyarthritis
4	Spondylitis
5	Arthritis mutilans

CASPAR score

1	Skin psoriasis present -	2
	Past -	1
	Fa/h If pt not affected -	1
2	Nail (pits/ onycholysis/ hyperkeratosis)	1
3	Dactylitis	1
4	Rheumatoid factor negative	1
5	Juxtaarticular new bone formation	1

Annexure 4 - Clinical research form for controls

CLINICAL RESEARCH FORM

Vitamin D deficiency and Psoriasis Vulgaris

Study ID ☐☐☐ Hospital Num. ☐☐☐☐☐☐☐ Date _ _ / _ _ / 201 _

Age ☐☐ Sex (1-M, 2-F) ☐ Locality (1-Urban, 2-Semi-Urban, 3-Rural) ☐

Occupation (1-Outdoor, 2-Indoor) ☐ Fitzpatrick Skin Type (3, 4, 5, 6) ☐

Avg. Sun hours: week day (hh:mm) ☐☐:☐☐ week end (hh:mm) ☐☐:☐☐

Sun screen usage (1-Always, 2-Mostly, 3-Occasional, 4-Never) ☐ SPF (if used) ☐☐

Clothing (1 Face, 2 Hand/Feet/Neck, 3 Forearms, 4 Waist, 5 Legs) ☐

Family history of Psoriasis (1-Yes, 0-No, 2-Doubtful) ☐

Smoking (1-Yes, 0-No) ☐ If yes, avg. Cigars/day ☐☐.☐☐ No. of years ☐☐

Alcohol (1-Yes, 0-No) ☐ If yes, frequency (1-Daily, 2-Weekly, 3-Monthly, 4-Occational ☐

Avg. quantity alcohol/week (in ml.) ☐☐☐☐ No. of years of alcohol ☐☐

Avg./week: Fish (gms) ☐☐☐☐ Milk (ml) ☐☐☐☐ Milk fortified (1-Yes,0-No) ☐

Diabetic (1-Y,0-N) ☐ If yes, num yrs ☐☐.☐☐ Treatment (1-Drugs, 2-Diet) ☐

Hypertensive (1-Yes, 0-No) ☐ If yes, duration (in years) ☐☐.☐☐

Dyslipidemia (1-Yes, 0-No) ☐ If yes, treatment (1-Drugs, 2-Diet control) ☐

Weight (kg) ☐☐☐.☐☐ Height (cms) ☐☐☐ BMI ☐☐.☐☐

BP1 ☐☐☐/☐☐☐ BP2 ☐☐☐/☐☐☐ AC ☐☐☐ PC ☐☐☐

Waist (cms) ☐☐☐.☐ Total Cholesterol ☐☐☐ Triglycerides ☐☐☐

HDL ☐☐ LDL ☐☐☐ Vitamin D level ☐☐.☐☐

Is Control? (1-Yes, 0-No) ☐

Dermatological diagnosis: ☐☐ ----------

BSA Percentage: ☐☐.☐☐

Annexure 5 – Criteria for metabolic syndrome and central obesity

Table 1: The new International Diabetes Federation (IDF) definition

According to the new IDF definition, for a person to be defined as having the metabolic syndrome they must have:

Central obesity (defined as waist circumference* with ethnicity specific values)

plus any two of the following four factors:

Raised triglycerides	≥ 150 mg/dL (1.7 mmol/L) **or specific treatment for this lipid abnormality**
Reduced HDL cholesterol	< 40 mg/dL (1.03 mmol/L) in males < 50 mg/dL (1.29 mmol/L) in females **or specific treatment for this lipid abnormality**
Raised blood pressure	systolic BP ≥ 130 or diastolic BP ≥ 85 mm Hg **or treatment of previously diagnosed hypertension**
Raised fasting plasma glucose	(FPG) ≥ 100 mg/dL (5.6 mmol/L), **or previously diagnosed type 2 diabetes** If above 5.6 mmol/L or 100 mg/dL, OGTT is strongly recommended but is not necessary to define presence of the syndrome.

** If BMI is >30kg/m², central obesity can be assumed and waist circumference does not need to be measured.*

Table 2: Ethnic specific values for waist circumference

Country/Ethnic group		Waist circumference
Europids* In the USA, the ATP III values (102 cm male; 88 cm female) are likely to continue to be used for clinical purposes	Male	≥ 94 cm
	Female	≥ 80 cm
South Asians Based on a Chinese, Malay and Asian-Indian population	Male	≥ 90 cm
	Female	≥ 80 cm
Chinese	Male	≥ 90 cm
	Female	≥ 80 cm
Japanese**	Male	≥ 90 cm
	Female	≥ 80 cm
Ethnic South and Central Americans	Use South Asian recommendations until more specific data are available	
Sub-Saharan Africans	Use European data until more specific data are available	
Eastern Mediterranean and Middle East (Arab) populations	Use European data until more specific data are available	

** In future epidemiological studies of populations of Europid origin, prevalence should be given using both European and North American cut-points to allow better comparisons.*

*** Originally different values were proposed for Japanese people but new data support the use of the values shown above.*

Annexure 6 – Master chart

Study id	Date	Age	Sex	Locality	Occupation	Skin type	wkdaysunhr	wkendsunhr	sunscreen	SPF	Clothing	Family history	Smoking	Cigar./day	Cigar years	Alcohol	Alc. Freq.	Avg. ml/week	Yrs. of alcohol	Fish/week	Milk/day	Fortified	Diabetic	DM duration	DM treatment
P01	28/01/2014	33	2	3	1	5	7	1	4		4	0	0			0				0	200	0	0		
P02	15/02/2014	27	2	2	2	4	0.3	0.3	4		3	0	0			0				500	100	0	0		
P03	22/02/2014	20	2	2	1	4	2	1	4		4	0	0			0				200	200	0	0		
P04	22/02/2014	20	2	3	2	5	0.15	0.3	4		3	0	0			0				50	200	0	0		
P05	22/02/2014	34	1	3	2	5	2	0.3	4		2	0	1	5	5	1	4	50	2	100	250	0	0		
P06	27/02/2014	42	1	3	1	5	8	2	4		3	0	0			0				0	100	0	0		
P07	27/02/2014	24	1	2	2	4	2	0.3	4		2	0	0			0				0	250	0	0		
P08	01/03/2014	27	1	2	2	5	1	0.3	4		3	0	0			0				200	300	0	0		
P09	04/03/2014	21	1	2	2	5	8	3	4		3	0	0			0				50	200	0	0		
P10	06/03/2014	44	2	3	2	4	0.3	1	4		4	0	0			0				0	300	0	0		
P11	08/03/2014	51	2	3	2	5	0.15	0.3	4		4	0	0			0				50	500	0	0		
P12	22/02/2014	54	2	2	2	5	0.15	1	4		4	0	0			0				600	400	0	0		
P13	18/03/2014	44	1	3	1	5	5	3	4		3	0	0			0				0	300	0	0		
P14	18/03/2014	44	1	2	1	5	5	2	4		3	0	0			1	2	200	2	100	200	0	0		
P15	22/03/2014	59	1	2	2	5	0.3	0.3	4		2	0	0			0				0	300	0	1	1	1
P16	01/04/2014	35	1	3	2	5	1	1	4		3	0	0			0				50	100	0	0		
P17	01/04/2014	37	1	3	1	5	3	2	4		2	1	0			0				50	250	0	0		
P18	01/04/2014	44	1	3	2	4	0.3	0.3	4		2	0	0			0				100	300	0	1	4	1
P19	08/04/2014	59	1	2	1	5	8	6	4		3	0	0			1	4	50	10	0	300	0	1	1	1
P20	26/04/2014	50	1	3	2	5	1	2	4		2	0	0			0				0	300	0	0		
P21	24/04/2014	60	1	3	2	5	2	2	4		2	0	0			0				100	200	0	1	8	1
P22	01/05/2014	27	2	2	2	5	0.15	0.3	4		4	0	0			0				100	500	0	0		
P23	05/06/2014	36	1	2	1	5	5	5	4		3	0	0			0				0	400	0	0		
P24	06/06/2014	39	1	3	1	5	3	2	4		3	0	0			1	4	10	5	0	200	0	0		
P25	06/06/2014	28	1	2	2	5	2	3	4		2	0	0			1	4	5	3	200	400	0	0		
P26	10/06/2014	51	2	3	1	5	4	4	4		4	0	0			0				0	300	0	0		
P27	12/06/2014	54	1	2	1	5	0.3	0.3	4		3	0	0			0				0	200	0	1	4	2
P28	14/06/2014	36	2	3	1	5	3	1	4		4	0	0			0				0	100	0	0		
P29	14/06/2014	33	1	2	1	5	1	2	4		2	0	1	1	2	0				0	300	0	0		
P30	17/06/2014	62	2	2	2	4	0.3	0.3	4		1	0	0			0				0	100	0	1	10	1
P31	17/06/2014	25	2	2	2	5	1	1	4		3	0	0			0				0	300	0	0		
P32	17/06/2014	65	1	3	1	5	8	8	4		3	0	0			1	4	50	5	0	200	0	0		
P33	28/06/2014	44	1	3	1	5	8	2	4		5	1	0			1	4	50	15	0	200	0	0		

Study id	Date	Age	Sex	Locality	Occupation	Skin type	wkdaysunhr	wkendsunhr	sunscreen	SPF	Clothing	Family history	Smoking	Cigar./day	Cigar years	Alcohol	Alc. Freq.	Avg. ml/week	Yrs. of alcohol	Fish/week	Milk/day	Fortified	Diabetic	DM duration	DM treatment
P34	28/06/2014	56	2	2	2	4	0.15	0.15	4		4	0	0			0				200	150	0	0		
P35	28/06/2014	30	2	2	2	4	0.1	0.1	4		1	0	0			0				100	250	0	0		
P36	01/07/2014	38	1	1	2	5	0.3	0.3	4		2	1	0			0				0	0	0	0		
P37	03/07/2014	59	1	2	2	5	0.2	0.3	4		2	1	1	4	10	1	3	25	8	200	350	0	1	14	1
P38	03/07/2014	50	2	2	2	4	0.3	0.3	4		4	0	0			0				150	250	0	1	0.25	2
P39	03/07/2014	59	2	3	2	5	0.15	0.3	4		4	1	0			0				50	300	0	0		
P40	03/07/2014	40	1	2	1	5	5	4	4		2	0	1	3	15	0				0	250	0	0		
P41	03/07/2014	34	2	3	2	5	0.3	2	4		4	0	0			0				200	400	0	0		
P42	05/07/2014	35	2	3	1	5	6	2	4		4	0	0			0				0	200	0	0		
P43	08/07/2014	41	2	3	1	5	5	4	4		4	0	0			0				50	250	0	0		
P44	10/07/2014	57	1	2	1	5	2	1	4		3	1	0			0				150	300	0	0		
P45	10/07/2014	48	1	2	2	5	0.3	0.3	4		2	0	1	2	20	0				0	300	0	1	10	1
P46	12/07/2014	41	1	2	1	5	5	4	4		2	0	0			0				0	300	0	0		
P47	12/07/2014	48	1	3	2	5	1	0.3	4		3	0	0			0				0	350	0	0		
P48	13/03/2014	56	1	2	2	5	0.3	0.3	4		3	0	0			0				0	200	0	0		
P49	17/07/2014	51	2	2	2	5	0.3	0.3	4		4	0	0			0				100	0	0	1	10	1
P50	22/07/2014	26	1	3	1	5	6	5	4		3	0	0			1	4	10	3	0	0	0	0		
P51	02/08/2014	35	1	2	2	4	1	1	4		2	0	1	12	10	0				50	150	0	0		
P52	05/08/2014	44	2	3	1	5	0.3	0.3	4		4	0	0			0				100	300	0	1	6	1
P53	14/08/2014	59	1	2	2	4	0.3	0.3	4		3	0	0			1	1	630	2	50	0	0	1	5	1
C01	03/06/2014	20	2	2	2	4	0.3	1	3	15	3	0	0			0				0	300	0	0		
C02	05/06/2014	44	1	2	2	4	0.3	1	4		2	0	0			0				50	400	0	0		
C03	10/06/2014	53	2	3	2	5	0.3	1	4		4	0	0			0				100	100	0	1	2	1
C04	10/06/2014	53	1	3	1	5	8	8	4		5	0	0			0				100	200	0	0		
C05	17/06/2014	42	2	3	1	5	8	5	4		4	0	0			0				0	50	0	0		
C06	17/06/2014	31	2	2	2	4	1	0.3	4		4	0	0			0				50	150	0	0		
C07	17/06/2014	46	1	2	2	5	0.1	1	4		3	0	0			0				200	150	0	0		
C08	17/06/2014	33	1	3	1	5	8	6	4		5	0	0			0				50	50	0	0		
C09	19/06/2014	34	1	2	1	5	8	6	4		3	0	0			0				0	300	0	0		
C10	21/06/2014	18	2	2	2	5	0.3	0.3	4		3	0	0			0				100	250	0	0		
C11	24/06/2014	50	2	2	2	4	0.3	0.3	4		4	0	0			0				0	300	0	1	5	1
C12	24/06/2014	27	2	3	1	5	2	1	4		4	0	0			0				0	50	0	0		
C13	24/06/2014	24	1	2	1	5	6	1	4		2	0	0			0				0	150	0	0		

Study id	Date	Age	Sex	Locality	Occupation	Skin type	wkdaysunhr	wkendsunhr	sunscreen	SPF	Clothing	Family history	Smoking	Cigar./day	Cigar years	Alcohol	Alc. Freq.	Avg. ml/week	Yrs. of alcohol	Fish/week	Milk/day	Fortified	Diabetic	DM duration	DM treatment
C14	26/06/2014	24	1	2	1	5	1	1	4		3	0	0			0				200	250	0	0		
C15	01/07/2014	34	2	2	1	4	0.2	0.2	4		4	0	0			0				0	200	0	0		
C16	01/07/2014	52	1	2	1	5	2	1	4		3	0	1	3	20	0				50	300	0	0		
C17	01/07/2014	35	1	2	2	5	0.15	0.3	3	15	2	0	0			0				100	250	0	0		
C18	03/07/2014	30	1	2	1	5	6	6	4		3	0	0			0				0	250	0	0		
C19	03/07/2014	37	1	2	2	5	2	1	4		3	0	0			0				50	400	0	1	3	1
C20	03/07/2014	32	1	2	2	4	0.15	0.3	4		3	0	0			0				0	100	0	0		
C21	12/07/2014	52	2	3	2	5	0.3	0.3	4		4	0	0			0				100	200	0	0		
C22	17/07/2014	52	2	3	1	5	6	6	4		4	0	0			0				150	300	0	0		
C23	17/07/2014	24	2	2	2	4	0.3	0.3	4		4	0	0			0				0	250	0	0		
C24	22/07/2014	35	2	2	2	5	0.2	0.2	2	30	3	0	0			0				50	350	0	0		
C25	24/07/2014	27	1	2	2	5	3	3	4		3	0	0			0				0	300	0	0		
C26	02/08/2014	37	1	3	1	5	6	6	4		5	0	0			0				0	200	0	0		
C27	05/08/2014	60	1	3	1	5	6	6	4		5	0	0			0				0	150	0	0		
C28	05/08/2014	37	2	2	2	4	0.3	1	4		4	0	0			0				100	200	0	0		
C29	07/08/2014	34	2	3	2	5	1	2	4		4	0	0			0				100	200	0	0		
C30	12/08/2014	39	2	2	2	4	0.3	0.3	4		3	0	0			0				0	100	0	0		
C31	12/08/2014	44	1	2	2	5	1	1	4		3	0	1	5	25	0				0	300	0	0		
C32	03/07/2014	21	1	2	2	5	0.3	0.3	4		3	0	0			0				0	250	0	0		
C33	14/08/2014	25	2	3	2	5	0.45	0.3	4		4	0	0			0				0	250	0	0		
C34	14/08/2014	41	1	3	1	4	8	8	4		5	0	1	5	15	1	2	90	8	0	300	0	0		
C35	14/08/2014	39	1	3	1	5	3	3	4		3	0	0			0				0	300	0	0		
C36	13/08/2014	42	2	3	2	5	0.3	0.3	4		4	0	0			0				50	600	0	0		
C37	16/08/2014	38	1	2	1	5	2	2	4		3	0	1	10	15	0				100	300	0	0		
C38	16/08/2014	58	2	2	2	4	0.3	0.3	4		4	0	0			0				100	300	0	0		
C39	21/08/2014	42	1	2	2	5	0.3	1	4		3	0	0			0				50	200	0	1	2	1
C40	21/08/2014	59	1	2	2	5	1	1	4		3	0	1	20	25	0				100	350	0	0		
C41	21/08/2014	52	1	2	2	5	2	3	3	26	3	0	0			0				50	200	0	1	5	1
C42	26/08/2014	57	1	3	1	5	8	8	4		3	0	0			0				100	200	0	0		
C43	26/08/2014	46	1	2	1	5	0.3	0.3	4		2	0	1	10	30	1	4	30	30	0	450	0	1	12	1
C44	26/08/2014	64	2	2	2	5	0.3	0.3	4		4	0	0			0				0	300	0	0		
C45	26/08/2014	46	1	2	1	5	6	5	4		2	0	0			0				0	100	0	1	1	1
C46	29/08/2014	59	1	3	1	5	5	4	4		3	0	0			0				0	250	0	0		
C47	30/08/2014	65	1	2	2	5	1	1	4		3	0	0			0				0	300	0	0		

Study id	Hypertension	HT duration	Dyslipidemia	Dys. Treatment	Weight	Height	BMI	SBP1	DBP1	SBP1	DBP1	Waist	AC	PC	Cholesterol	Triglycerides	HDL	LDL	Vitamin D
P01	0		0		65	158	26	100	70	110	70	78	82	126					30.7
P02	0		0		64	156	26.3	116	70	110	70	88	90	103	138	67	48	82	11.57
P03	0		0		57.5	151	25.2	116	70	110	70	81	102	111	137	89	27	93	28.93
P04	0		0		40	154	16.9	100	70	96	70	64	74	84	102	68	35	58	10.65
P05	0		0		61	174	20.1	140	70	146	78	85							
P06	0		0		50	161	19.3	110	80	110	76	77	93	97	124	80	43	69	16.37
P07	0		0		61	165	22.4	110	70	106	70	78	93	91	221	126	46	152	18.2
P08	0		0		64	163	24.1	120	80	120	76	81	111	136	204	251	49	136	
P09	0		0		54	163	20.3	116	80	110	76	72	81	81	159	152	34	110	17.73
P10	0		0		103	160	40.2	160	90	150	90	112	85	90	156	94	40	99	17.6
P11	0		0		74	159	29.3	100	70	100	70	94							
P12	0		0		64	160	25	140	84	140	90	90	115	119	197	80	48	122	28.6
P13	0		0		64	170	22.1	110	84	110	86	82							
P14	0		0		70	165	25.7	124	80	120	80	94	92	102	125	63	33	84	39.37
P15	1	3	0		84	163	31.6	150	96	150	90	110	162	216	113	69	38	64	5.92
P16	0		0		84	167	30.1	140	90	140	90	102	151	138	218	270	36	149	15.78
P17	0		0		83	178	26.2	140	100	140	100	99	88	89	194	118	42	138	21.58
P18	1	4	1	1	67	167	24	150	96	150	90	90	139	129	129	228	51	71	14.02
P19	1	2	1	1	83	172	28.1	150	96	156	90	107	107	249	167	134	40	105	
P20	0		0		80	164	29.7	140	94	140	96	100	90	111	188	210	32	124	19.44
P21	0		1	1	70	162	26.7	130	80	130	80	96	110	126	157	185	39	99	19.62
P22	0		0		63.5	165	23.3	130	86	130	80	75	85	112	120	64	30	86	20.66
P23	0		0		67	167	24	130	80	130	80	87	85	96	160	63	53	101	18.33
P24	0		0		76	164	28.3	120	80	120	76	98	91	113	198	76	40	137	32.57
P25	0		0		74	187	21.2	150	100	130	90	80	87	109	217	137	48	149	29.07
P26	0		0		68	161	26.2	156	100	150	100	84	95	107	182	111	47	116	40.48
P27	0		0		89	167	31.9	140	100	140	100	115	121	258	232	107	54	162	17.38
P28	0		0		73	159	28.9	120	70	114	70	90	84	105	110	116	25	72	20.36
P29	0		0		63	165	23.1	120	80	120	80	90							
P30	1	8	1	2	85	162	32.4	150	100	150	96	96	205	239	162	225	31	104	7.02
P31	0		0		103	156	42.3	156	100	150	100	102	102	104	142	73	36	96	8.41
P32	0		0		45	157	18.3	130	80	130	80	73	101	113	147	72	32	112	36.24
P33	0		0		75	168	26.6	110	80	110	80	99	87	111	217	134	55	148	49.67

Study id	Hypertension	HT duration	Dyslipidemia	Dys. Treatment	Weight	Height	BMI	SBP1	DBP1	SBP1	DBP1	Waist	AC	PC	Cholesterol	Triglycerides	HDL	LDL	Vitamin D
P34	0		0		77.5	158	31	130	80	124	78	95	101	105					
P35	0		0		58	162	22.1	110	70	106	70	81	91	87	142	125	35	95	15.8
P36	0		0		95	170	32.9	140	100	142	96	111	89	70	170	115	36	122	9.22
P37	0		0		70	159	27.7	124	80	120	80	98							
P38	1	10	1	1	71	153	30.3	170	100	160	100	94	119	181	109	106	42	56	16.12
P39	0		1	2	69	144	33.3	150	90	150	86	94	99	110	208	125	47	144	12.14
P40	0		0		84	178	26.5	140	80	140	76	105		116					5.19
P41	1	0.25	0		94	150	41.8	160	106	156	104	101	103	99	186	78	38	129	15.98
P42	0		0		67	154	28.3	120	80	120	76	92	239	230	133	546	24	44	18.7
P43	0		0		55	153	23.5	110	80	110	74	74	89	103	151	120	51	95	26.91
P44	0		0		102	175	33.3	140	90	146	90	118	105	156	208	88	44	152	17.87
P45	0		0		83	165	30.5	140	100	146	100	114	116	203	199	263	36	139	15.79
P46	0		0		63	157	25.6	130	90	130	84	90	105	121	194	288	36	136	19.32
P47	0		0		65	170	22.5	170	110	160	110	94		255					37.05
P48	1	1.5	1	1	68	162	25.9	130	80	120	76	84	97	140	158	187	41	86	28.81
P49	0		1	1	69	150	30.7	130	80	134	80	92	107	122	137	144	54	80	22.99
P50	0		0		57	157	23.1	120	74	120	70	79	76	86	234	193	63	161	53.89
P51	0		0		59	175	19.3	120	70	120	66	75	78	81	189	117	34	139	10.19
P52	0		0		56	158	22.4	150	80	146	80	77	143	229	180	99	55	110	17.48
P53	1	3	1	1	80	165	29.4	130	100	130	96	105	175	210	167	153	31	113	15.91
C01	0		0		74	170	25.6	106	70	100	70	79	77	74	116	40	52	63	8.21
C02	0		0		72	173	24.1	110	80	110	80	88	90	101	235	189	35	175	11.17
C03	0		0		90	160	35.2	120	80	120	80	105	106	152	128	129	36	83	34.51
C04	0		0		45	160	17.6	120	80	120	80	70	83	148	190	86	64	112	51.62
C05	0		0		52	165	19.1	120	70	114	70	66	77	89	99	38	46	60	22.16
C06	0		0		59	157	23.9	120	70	124	66	82	82	107	133	54	31	94	29.52
C07	0		1	2	65	165	23.9	140	90	130	82	84	135	128	187	182	37	134	15.16
C08	0		0		55	161	21.2	120	84	120	84	82	159	202	177	107	46	124	16.92
C09	0		0		84	164	31.2	160	100	152	100	92	86	102	143	101	29	98	21.24
C10	0		0		40	153	17.1	100	70	104	70	57	81	80	135	64	42	85	12.72
C11	0		0		60	153	25.6	150	96	150	90	88	143	171	201	241	30	161	13.95
C12	0		0		40	147	18.5	120	76	120	70	60	85	86	122	35	46	75	22.76
C13	0		0		75	186	21.7	110	76	110	70	86	89	95	162	90	47	106	11.47

Study id	Hypertension	HT duration	Dyslipidemia	Dys. Treatment	Weight	Height	BMI	SBP1	DBP1	SBP1	DBP1	Waist	AC	PC	Cholesterol	Triglycerides	HDL	LDL	Vitamin D
C14	0		0		85	174	28.1	140	80	132	84	98							
C15	0		0		81	162	30.9	120	80	116	80	92	93	98	181	196	32	128	14.89
C16	0		0		65	163	24.5	120	70	120	76	94	104	180	181	78	28	139	16.42
C17	0		1	2	79	178	24.9	120	80	120	80	95	93	114	163	116	21	82	13.46
C18	0		0		60	171	20.5	110	80	110	80	86	88	135	138	73	51	87	22.4
C19	0		0		85	161	32.8	100	76	100	80	108							31.65
C20	0		0		105	174	34.7	120	90	120	86	111	100	113	178	63	51	117	13.85
C21	0		0		69	160	27	110	70	110	74	88	96	106	199	135	40	139	31.04
C22	0		0		64	152	27.7	110	70	104	70	91	111	86	223	163	34	169	30.52
C23	0		0		57.5	156	23.6	120	76	126	70	80							17.81
C24	0		0		45	152	19.5	90	70	90	70	64	93	91	165	44	61	102	13.63
C25	0		0		62	165	22.8	120	70	116	70	86	105	89	195	102	39	135	16.04
C26	0		0		59	164	21.9	110	70	100	70	81	87	105	152	80	35	103	23.47
C27	0		0		55	165	20.2	120	80	120	76	71	85	189	181	95	41	125	24.8
C28	0		0		88	165	32.3	130	80	130	80	94	102	93	157	65	37	100	31.15
C29	0		0		60	161	23.1	120	76	120	70	82	87	105	190	59	55	122	28.83
C30	0		0		55	153	23.5	120	80	120	80	79	94	71	186	153	44	119	43.34
C31	0		0		62.5	162	23.8	130	90	130	86	84	101	186	157	108	37	101	10.7
C32	0		0		75	169	26.3	120	80	120	80	74		82	191	86	57	127	15.57
C33	0		0		50	155	20.8	110	70	100	70	70							20.1
C34	0		0		80	169	28	110	80	110	80	97	109	98	216	205	46	157	16.99
C35	0		0		67.5	165	24.8	120	80	120	80	88		86					23.85
C36	0		0		102	167	36.6	130	80	126	80	98	95	97	159	101	34	109	20.06
C37	0		0		102	168	36.1	150	110	150	106	116	81	98	197	169	28	139	24.57
C38	0		0		74	156	30.4	120	70	120	76	90	91		206	120	33	147	21.23
C39	0		0		64	168	22.7	130	84	130	80	80	106	88	141	328	25	83	6.02
C40	0		0		57	165	20.9	120	80	120	80	80	93	167	155	69	24	111	28.28
C41	0		0		75	170	26	130	78	130	80	86	92	177	136	111	47	79	9.28
C42	0		0		64	178	20.2	120	90	120	86	84	86	85	141	56	43	90	26.89
C43	0		1	1	72	168	25.5	120	80	116	80	90	79	180	99	114	35	55	16.56
C44	1	1	0		55	149	24.8	110	70	110	74	90	85	122	198	111	52	134	26
C45	0		0		60	170	20.8	130	86	130	80	84	116	136	134	235	33	75	12.17
C46	0		0		56	162	21.3	130	70	130	80	81	95	138	116	88	35	73	23.23
C47	0		0		54	158	21.6	120	80	114	76	80	99	115	175	100	46	121	36.76

Study id	Is control?	Derm. Diagnosis	BSA %	Onset age	Season	Avoidance	Reason	Topical Rx	Nail invol.	NAPSI	Arthritis	CASPAR	Moll Wright	Symptomatic	BSA invol.	PASI
P01	0			24	0	0		1	1	2	1	4	3	1	30	15.6
P02	0			12	0	0		1	1	2	0				5	5
P03	0			17	1	0		1	1	1	0				20	8.9
P04	0			19	0	0		3	1	3	0				8	2.4
P05	0			32	1	1	1	5	1	6	0				15	7.5
P06	0			30	0	0	0	8	1	6	0				10	6.3
P07	0			21	1	1	1	8	1	22	0				5	6.4
P08	0			26	0	0	0	2	1	3	0				5	4.1
P09	0			5	1	0	0	1	1	2	0				20	10.3
P10	0			41	0	0		2	1	4	0				5	3.2
P11	0			48	0	0		2	1	4	0				5	5.2
P12	0			18	1	0		2	1	3	0				10	4.7
P13	0			42	1	0		3	1	29	0				8	4.1
P14	0			40	0	0		1	1	6	0				8	7.2
P15	0			56	2	0		8	0		0				4	1.4
P16	0			30	1	1	1	7	1	7	0				5	6.1
P17	0			28	1	1	1	7	1	10	0				50	15.6
P18	0			37	0	0		5	1	1	0				5	5.6
P19	0			55	2	0		7	1	4	0				8	5.3
P20	0			23	1	1	1	8	1	7	0				5	3.2
P21	0			45	1	0		1	0		0				3	2
P22	0			25	1	0		1	0		0				3	3.3
P23	0			34	2	0		7	1	20	0				4	3
P24	0			25	2	1	1	8	1	14	1	4	3	1	5	4.5
P25	0			25	2	0		2	0		0				3	1.6
P26	0			49	1	0		2	1	5	0				5	2.2
P27	0			30	2	1	1	6	1	5	0				10	8
P28	0			33	0	0		6	0		0				5	3
P29	0			28	0	0		1	1	22	1	4	2	1	5	2.6
P30	0			10	0	0		1	1	1	0				3	1.6
P31	0			12	1	1	1	2	0		0				8	5
P32	0			60	0	1	1	7	1	15	0				35	16.2
P33	0			40	0	0		2	1	1	0				6	4.8

Study id	Is control?	Derm. Diagnosis	BSA %	Onset age	Season	Avoidance	Reason	Topical Rx	Nail invol.	NAPSI	Arthritis	CASPAR	Moll Wright	Symptomatic	BSA invol.	PASI
P34	0			52	1	0		1	0		0				5	5.2
P35	0			26	0	0		2	1	6	0				4	4
P36	0			15	1	0		2	1	4	0				3	2
P37	0			35	0	0		1	0		0				4	5.2
P38	0			35	0	0		3	0		0				4	2.4
P39	0			25	1	0		2	1	6	0				5	4.6
P40	0			17	2	1	1	1	1	11	1	2	4	1	15	7.2
P41	0			34	0	0		1	0		0				8	6.6
P42	0			31	0	0		1	1	37	0				7	7.4
P43	0			35	1	0		1	0		0				4	4
P44	0			50	0	0		8	0		0				3	3
P45	0			40	0	0		2	1	3	0				3	2
P46	0			35	1	1	1	6	0		0				3	0.9
P47	0			38	0	0		7	1	15	0				8	6.7
P48	0			52	1	0		2	1	6	1	5	2	1	2	1.5
P49	0			46	1	1	1	1	0		0				5	4.6
P50	0			24	0	1	1	2	0		0				12	7.4
P51	0			34	0	1	1	2	1	3	0				8	6.4
P52	0			22	1	1	1	2	0		1	4	3	1	5	5.6
P53	0			58	0	0		1	0		0				4	3.6
C01	1	1	1													
C02	1	1	1													
C03	1	2	1													
C04	1	1	5													
C05	1	3	0													
C06	1	2	1													
C07	1	4	1													
C08	1	2	1													
C09	1	1	2													
C10	1	1	1													
C11	1	2	1													
C12	1	5	1													
C13	1	6	2													

Study id	Is control?	Derm. Diagnosis	BSA %	Onset age	Season	Avoidance	Reason	Topical Rx	Nail invol.	NAPSI	Arthritis	CASPAR	Moll Wright	Symptomatic	BSA invol.	PASI
C14	1	7	1													
C15	1	2	1													
C16	1	8	1													
C17	1	9	1													
C18	1	1	5													
C19	1	10	1													
C20	1	11	1													
C21	1	1	1													
C22	1	8	3													
C23	1	8	2													
C24	1	12	1													
C25	1	13	2													
C26	1	8	2													
C27	1	14	2													
C28	1	15	1													
C29	1	14	2													
C30	1	7	1													
C31	1	1	3													
C32	1	10	1													
C33	1	16	1													
C34	1	17	5													
C35	1	11	1													
C36	1	12	2													
C37	1	17	5													
C38	1	9	1													
C39	1	6	3													
C40	1	7	1													
C41	1	15	1													
C42	1	7	1													
C43	1	1	4													
C44	1	15	1													
C45	1	18	1													
C46	1	7	1													
C47	1	7	1													

Age and sex matched pairs of cases and controls:

Pair ID	Study ID	Age	Sex	Case/Ctrl	Pair ID	Study ID	Age	Sex	Case/Ctrl	Pair ID	Study ID	Age	Sex	Case/Ctrl
1	P01	33	Female	case	16	P21	60	Male	case	31	P39	59	Female	case
1	C15	34	Female	control	16	C40	59	Male	control	31	C38	58	Female	control
2	P02	27	Female	case	17	P22	27	Female	case	32	P40	40	Male	case
2	C33	25	Female	control	17	C12	27	Female	control	32	C35	39	Male	control
3	P03	20	Female	case	18	P23	36	Male	case	33	P41	34	Female	case
3	C01	20	Female	control	18	C09	34	Male	control	33	C24	35	Female	control
4	P04	20	Female	case	19	P24	39	Male	case	34	P42	35	Female	case
4	C10	18	Female	control	19	C19	37	Male	control	34	C28	37	Female	control
5	P06	42	Male	case	20	P25	28	Male	case	35	P43	41	Female	case
5	C34	41	Male	control	20	C18	30	Male	control	35	C30	39	Female	control
6	P07	24	Male	case	21	P26	51	Female	case	36	P44	57	Male	case
6	C13	24	Male	control	21	C11	50	Female	control	36	C42	57	Male	control
7	P09	21	Male	case	22	P27	54	Male	case	37	P45	48	Male	case
7	C32	21	Male	control	22	C41	52	Male	control	37	C43	46	Male	control
8	P10	44	Female	case	23	P28	36	Female	case	38	P46	41	Male	case
8	C05	42	Female	control	23	C29	34	Female	control	38	C39	42	Male	control
9	P12	54	Female	case	24	P30	62	Female	case	39	P47	48	Male	case
9	C03	53	Female	control	24	C44	64	Female	control	39	C45	46	Male	control
10	P14	44	Male	case	25	P31	25	Female	case	40	P48	56	Male	case
10	C02	44	Male	control	25	C23	24	Female	control	40	C04	54	Male	control
11	P15	59	Male	case	26	P32	65	Male	case	41	P49	51	Female	case
11	C27	60	Male	control	26	C47	65	Male	control	41	C21	52	Female	control
12	P16	35	Male	case	27	P33	44	Male	case	42	P50	26	Male	case
12	C08	33	Male	control	27	C31	44	Male	control	42	C25	27	Male	control
13	P17	37	Male	case	28	P35	30	Female	case	43	P51	35	Male	case
13	C26	37	Male	control	28	C06	31	Female	control	43	C17	35	Male	control
14	P18	44	Male	case	29	P36	38	Male	case	44	P52	44	Female	case
14	C07	46	Male	control	29	C37	38	Male	control	44	C36	42	Female	control
15	P20	50	Male	case	30	P38	50	Female	case	45	P53	59	Male	case
15	C16	52	Male	control	30	C22	52	Female	control	45	C46	59	Male	control

Keys to Master chart

1. Study id — Study identification number
   - P01 to P53 - Cases
   - C01 to C47 - Controls
2. Date — Date of recruitment
   - <dd/mm/yyyy>
3. Age — Age in years
4. Sex — Gender
   - 1 male, 2 female
5. Locality — Locality of the study subjects
   - 1 urban, 2 semi-urban, 3 rural
6. Occupation — Occupation of the subjects
   - 1 Outdoor, 2 Indoor
7. Skin type — Fitzpatrick Skin Type
8. wkdaysunhrs — Average hours of sun-exposure on week days (hh:mm)
9. wkendsunhrs — Average hours of sun-exposure on weekends (hh:mm)
10. sunscreen — Sunscreen usage pattern
    - 1 Always (Even Indoors), 2 Mostly (Avg. five days in a week), 3 Occasional (Not more than two days in a week), 4 Never
11. SPF — Sun protection factor
12. Clothing — Type of clothing while outdoor

- 1 Only face exposed (e.g. burqa), 2 Face, hands, feet & neck exposed (e.g. full sleeved shirt), 3 Forearms exposed (e.g. half sleeved shirt), 4 Waist exposed (e.g. sari), 5 Legs (e.g. dhoti only)

13. Family history — Family history of Psoriasis
    - 1 yes, 0 no, 2 doubtful
14. Smoking — Smoking
    - 1 yes, 0 no
15. Cigar./day — Average number of cigarettes smoked per day
16. Cigar years — Number of years of smoking
17. Alcohol — Alcohol consumption
    - 1 yes, 0 no
18. Alc. Freq. — Frequency of alcohol intake
    - 1 Almost daily, 2 Weekly, 3 Monthly, 4 Occasional
19. Avg. ml/week — Average quantity alcohol consumed per week (ml)
20. Yrs. of alcohol — Number of years of alcohol intake
21. Fish/week — Average quantity of fish intake per week (gm)
22. Milk/day — Average quantity of dairy products intake per day (ml)
23. Fortified — Whether milk is fortified?
    - 1 yes, 0 no
24. Diabetic — Is the subject a known diabetic

- 1 yes, 0 no

25. DM duration — Duration of diabetes in years

26. DM treatment — Treatment for diabetes

- 1 oral drugs, 2 only diet restriction, 3 insulin

27. Hypertension — Is the subject a known hypertensive

- 1 yes, 0 no

28. HT duration — Duration of hypertension (in years)

29. Dyslipidemia — Is the subject a known case of dyslipidemia

- 1 yes, 0 no

30. Dys. Treatment — Treatment for dyslipidemia

- 1 Drugs, 2 Diet Control

31. Weight — Weight (kg)

32. Height — Height (cm)

33. BMI — Body mass index

34. SBP1 — Systolic blood pressure 1 (mmHg)

35. DBP1 — Diastolic blood pressure 1 (mmHg)

36. SBP2 — Systolic blood pressure 2 (mmHg)

37. SBP2 — Diastolic blood pressure 2 (mmHg)

38. Waist — Waist circumference (cm)

39. AC — Fasting blood sugar (mg %)

40. PC — Post prandial blood sugar (mg %)

41. Cholesterol — Total Cholesterol (mg %)

42. Triglycerides	Triglycerides (mg %)
43. HDL	High density lipoprotein (mg %)
44. LDL	Low density lipoprotein (mg %)
45. Vitamin D	Vitamin D level (ng/ml)
46. Is control?	Is the subject recruited as control? - 1 yes, 0 no
47. Derm. Diagnosis	Dermatological diagnosis of controls 1 Superficial fungal infection, 2 Viral wart, 3 STI screening, 4 Herpes labialis, 5 Molluscum contagiosum, 6 Pityriasis capitis, 7 Fissures over heels, 8 Erythrasma, 9 Cherry angioma, 10 Keloid, 11 Zoons balanitis, 12 Acne grade1, 13 Androgenetic alopecia, 14 Post herpetic neuralgia, 15 Post inflammatory hyperpigmentation, 16 Black hairy tongue, 17 Pigmented purpuric dermatoses, 18 Corn
48. BSA %	Body surface area involved among controls (%)
49. Onset age	Age at onset of psoriasis (years)
50. Season	Seasonal exacerbation of psoriasis - 0 No seasonal change, 1 winter exacerbation, 2 summer exacerbation
51. Avoidance	Does patient avoid social activities due to psoriasis - 1 yes, 0 no
52. Reason	Reason for social avoidance

- 1 social reasons, 2 disability due to disease, 3 other reasons

53. Topical Rx — Topical treatment for psoriasis

- 1 Steroid, 2 Steroid + keratolytic, 3 Keratolytics, 4 Retinoids, 5 tar, 6 Only emollients, 7 Alternative forms of medicine, 8 No treatment in the last 3 months

54. Nail invol. — Are there any psoriatic nail changes?

- 1 yes, 0 no

55. NAPSI — NAPSI Score

56. Arthritis — Does the patient have arthritis?

- 1 yes, 0 no

57. CASPAR — CASPAR Score

58. Moll Wright — Moll and Wright classification of arthritis

- 1 Distal interphalangeal joints, 2 Asymmetric oligoarthritis, 3 Symmetric polyarthritis, 4 Spondyloarthritis, 5 Arthritis mutilans

59. Symptomatic — Is arthritis symptomatic now

- 1 yes, 0 no

60. BSA invol. — Total BSA involvement among cases (%)

61. PASI — Psoriasis area severity index score for cases